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Table of Contents.

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	Page.
ORIGINAL ARTICLES—	
The Criteria of a Cancer Cure, by W. E. Gye	869
The Importance of the Relativity of Blood Pressure and other Signs in the Prevention of Eclampsia, by T. Dixon Hughes	871
The Iron Losses of Healthy Women during Consecutive Menstrual Cycles, by Jean Millis	874
REVIEWS—	
Prothrombin Deficiency	879
Handbook of Psychology	879
NOTES ON BOOKS, CURRENT JOURNALS AND NEW APPLIANCES—	
Current Medicine	879
Exercises After Childbirth	880
Notes on Genetics	880
"The Cry and the Covenant"	880
BOOKS RECEIVED	880
LEADING ARTICLES—	
Skill and Age	881
CURRENT COMMENT—	
The Health of Ferrous Foundrymen	882
Subacute Bacterial Endocarditis	883
ABSTRACTS FROM MEDICAL LITERATURE—	
Pædiatrics	884
Orthopædic Surgery	885
RESEARCH—	
The Anti-Cancer Council of Victoria	886
OUT OF THE PAST	890
CORRESPONDENCE—	
Recurrent Pterygium	890
Modern Trends in Radiotherapy	890
Orthopædic Aspects of Rheumatoid Arthritis	891
Pre-Bronchiectasis	892
DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA	891
OBITUARY—	
George Alexander Eadie	892
NOTICE—	
The Sydney Institute for Psycho-Analysis	892
NOMINATIONS AND ELECTIONS	892
MEDICAL APPOINTMENTS	892
DIARY FOR THE MONTH	892
MEDICAL APPOINTMENTS: IMPORTANT NOTICE	892
EDITORIAL NOTICES	892

THE CRITERIA OF A CANCER CURE.

By W. E. GYE,
Perth.

(From the Cancer Research Laboratory of the Public Health Department of Western Australia.)

THE celebrated German pathologists of the nineteenth century—Virchow, Cohnheim, Ribbert—proved by the most meticulous microscopic examination of metastases, especially in lymph nodes, that the fundamental cause of cancer resides in the cancer cells themselves, since they grow and multiply independently of the body's needs. The probable mechanism of this continued multiplication does not concern us here, but it is of interest to consider how a knowledge of the fundamental pathological process can be applied to the problem of how to test and assess an alleged "cancer cure".

The practitioner faced with a case of cancer has at once two questions to consider, namely, how, if left to itself, will this cancer in all probability kill this patient and how can this predicted course be modified or avoided by treatment? The lethal complications which accompany the disease as it is presented in Nature are due to incidental factors, independent of the essential pathological process. They include, for example, sepsis, obstruction of a hollow organ, such as the gut, from within, pressure on vital organs, for example, the ureters, from without, interference with essential metabolic processes by destruction of liver tissue by metastases, interruption of essential nerve paths by pressure within the skull or on the spinal cord, interference with respiration by destruction of lung tissue or blocking of air passages, and loss of blood from ulceration into a large vessel. Only in very rare instances is a patient killed by the cancer *per se* and then only after an extremely long course, during which the extent and number of the cancer cells steadily increase until their distribution is virtually universal, but not lethal by virtue of interference at any one site. We therefore see that in order to prevent the patient dying of cancer we must prevent this mechanical interference with vital function, but in order to cure the cancer we must stop the uncontrolled cell multiplication. These are two problems, not one. The first is often solved by surgery, and by irradiation, the second is still unsolved but would be solved by a true "cancer cure".

The "killing" complications in man often act as "red herrings" in investigations of the results of treatment, since if they can be dealt with the patients' condition will be much ameliorated, but not cured. Let us see whether this problem of assessment of amelioration can be simplified.

Man as a Possible Laboratory Animal.

The protean manifestations and complications of the disease in man together with his average length of life make him an unsuitable laboratory animal, but can any other animal be used? Since the discoveries at the beginning of the century of the universal distribution of cancer in the vertebrates and of its exact similarity in animals and man, our investigations of it have been much simplified, and rats and mice form the most suitable subjects for tests. In the first place their life span is short enough to be easily observed, since any apparently cured cancer subject must be watched until death, and the cause of death ascertained. The usual five-year criterion in man is not sufficient, as is illustrated by a case observed by me recently. A middle-aged woman was admitted to hospital with a pleural effusion of sudden onset. There was no history of previous illness, but the patient remembered having a tumour removed from the skin of the neck twenty years before. The scar was barely visible. She died soon after, and the post-mortem examination revealed extensive secondary malignant melanomata in the hilar glands and pleura. The surgeon who removed the small skin primary may be forgiven if he had concluded for nineteen years that he had cured her.

Another example of the difficulty of judging whether a cancer has been cured is the following case. A schoolmistress in Guernsey was operated on by a German surgeon in 1898 (radical mastectomy for cancer of the breast). She recovered, returned to work and was completely well until 1913 when she slipped on the pavement and fractured a femur. X rays showed a secondary deposit. The patient was brought to London for observation and was found to have multitudes of skin nodules, the sections of which differed in no way from the sections of the tissue removed by the German surgeon fifteen years before. She died in 1914 with generalized carcinomatosis. Again the original surgeon would have been justified in claiming a cure.

It seems therefore imperative that animal experiment be linked with clinical observation.

Tests on Mice.

Fortunately it is now possible to test a "cancer cure" rationally on mice. So far it has not been possible to "cure" a mouse by any other means than complete surgical excision or radiation therapy. Operation is much more successful in animal tumours than is radiation therapy, since the majority of animal tumours are radio-resistant. This is also probably true in man since primary complete excision alone still offers 100% chance of cure. Once metastases are present or complete removal is impossible, the chances are unpredictable.

How does a mouse die of cancer? Are the complications as many as those in man? In most laboratory work the tumour is near the surface of the body. It ulcerates, becomes infected and the animal dies of sepsis, hæmorrhage, or perforation into a body cavity, before metastases have had time to appear. If, however, for example, a rat is inoculated with a sarcoma on the tail the tumour will grow very slowly, secondary deposits will occur in the liver and lungs *et cetera*, and the rat may die of liver failure or pneumonia or in any other way comparable to man.

How is a "cancer cure" tested on mice? In order to answer this we must consider the kinds of tumour available as raw material. Experimental tumours can be divided into two main classes—sporadic and induced. The commonest sporadic mouse tumour met with in laboratories is a hæmorrhagic adenocarcinoma of the breast. The cause of death in this type is the ulceration of the tumour, which kills by septic complications or hæmorrhage usually before metastases appear. Induced tumours are of two types, those tumours produced by inoculating tumour tissue from mouse to mouse (passaged) and those induced *de novo* by chemical carcinogens. Histologically both carcinomata and sarcomata are available (sporadic, passaged and chemically induced) for experimental purposes. There is therefore a wide range of choice possible when testing the therapeutic action of anything on a mouse cancer. But there are many pitfalls, and in order to understand the difficulty of assessing results we must consider how such tumour stocks have been built up.

Mouse Tumour Stocks and Hybrid Mice.

In the early days of cancer research large numbers of mice were kept and examined weekly. About 4% of these developed tumours. A "sporadic" tumour was removed by operation, and the tumour was then cut in very small pieces, each about 0·02 cubic centimetre in volume. The mouse in which the tumour had started was inoculated with one small piece at a site remote from the seat of origin, and as many as 50 to 100 normal mice were inoculated in the right flank with a fragment of the tumour. The "graft" in the original mouse always took and formed a "daughter" tumour. In the 50 or 100 normal mice a varying number, from 1% to 60%, of tumours developed. The most rapidly growing, the "best" of these tumours, was again transplanted to normal mice in the hope of getting a strain of tumour which would grow readily in a high percentage of mice inoculated. In this way were collected strains of tumours showing various histological appearances and biological variations which might prove to be of fundamental significance. For example, a strain of adenocarcinoma of a mouse was obtained which contained in its cytoplasm quite regularly granules of glycogen; another strain was propagated for at least thirty years, which grew rapidly for twelve days (a dose of 0·02 cubic centimetre yielded at twelve days 1·5 to 2·0 cubic centimetres of tumour) and thereafter softened rapidly, becoming fluid, and disappeared completely within ten days. This tumour had to be transplanted seven to ten days after inoculation, or it was lost.

It is obvious that if by any chance any "cure" for cancer had been tested in mice carrying such a tumour and without complete controls a "discovery" of apparently great importance would have been made. But other and more subtle difficulties beset the investigator. None of these tumours arising casually in mice which are not inbred—stock mice—and propagated in stock mice can be transmitted 100% to grow equally and regularly. A well-known tumour of rats, the Jensen rat sarcoma, which arose in a rat at the site where Jensen had injected tubercle bacilli, was for many years a test tumour. Yet this tumour rarely gives 100% takes, and frequently tumours which do start follow an irregular course and many disappear. It is therefore obvious that if this tumour is used to test a cancer cure a large number of rats must be treated and an equal number of control rats must be observed until they die. The action of the "cure" tested can then be assessed on a percentage basis of difference between treated and untreated animals.

The Twort tumour of mice behaves in a similarly erratic way, and at least one "cancer cure" on the market at the present time owes its reputation largely to the fact that this tumour was used in testing its action and that adequate control groups were not observed nor was evidence gathered from tests on other more stable tumours accepted by the manufacturers.

It is therefore obvious that what is required is a tumour of known rate of growth, which will take in 100% of cases when grafted from mouse to mouse, and if untreated, will kill the mouse in every instance. Such standard conditions are now available, through the building up of inbred strains of laboratory mice.

Inbred Strains of Mice.

Experimental brother-sister mating of mice was initiated in England in the laboratories of the Imperial Cancer Research Fund by J. A. Murray and carried to completion in the United States by Maude Slye, Leo Loeb and W. S. Murray during the first World War. The intention was to study the genetics of cancer, but in the course of the investigations which were duplicated in England, France and Holland many strains of inbred mice were created, which now after forty years can be considered stable and practically homozygous. These mice are of the greatest use in laboratory work. In any given strain homoplastic grafting (of skin or other normal tissue as well as of tumours) is successful in 100%, since there is no immune reaction between individuals. This alone makes these mice invaluable in cancer work since any number of similar tumours of similar weight and predictable rate of growth can be obtained for any experiment. In addition, the length of life, date of maturity, body weight, response to drugs and susceptibility to disease and to environmental conditions are constant within each strain. These mice therefore can be looked on as the "pure chemicals" or as the "clean test tubes" of animal experiment. Much smaller numbers are necessary to give an answer to any problem than if hybrid mice are used, and that answer is a clear-cut one.

Accurate experimental work on cancer would be impossible without such inbred mice. Some of the strains show a death rate of 95% in the females from cancer of the breast. In other strains it never occurs. It is possible also by selective breeding and by cross suckling (between the young of a high cancer line and a low cancer line foster mother and *vice versa*) to modify or to change this incidence completely, and it was in this way that the Bittner virus was discovered. However, we are not now concerned with the origin of cancer, but with the use of

these artificially created standard inbred mice in investigating cancer cures.

Desiderata of a Cancer Cure.

It is obvious that (surgery apart) the only requisite is that the substance shall prevent the continued division of the cancer cells and shall have no other effects. Let us consider the investigation of compounds of colchiceine, at one time thought to be such substances. If to ten of twenty inbred mice bearing tumours of the same size a single small dose of colchiceine is administered and all twenty are watched, it will be found that in the ten untreated controls the tumours continue to increase at a uniform rate and eventually kill the mouse, while in the ten treated mice the tumours cease growing at once, recede and often disappear. This at first sight looks to be just what we are hoping for, but as the experiment progresses it will be found that the ten treated mice die before the untreated ones, because mitosis has been stopped not only in the tumour cells but in all other cells as well, including those of the bone marrow. If the dose falls just short of this the mice may recover, but so will the tumour, and a second dose is invariably fatal. It is therefore not enough to kill the tumour cells—one must be sure that no other cells are killed as well.

Therefore in assessing the results of treatment in mice we must observe the following rules: (i) The mice must be inbred. (ii) The tumour must be one which takes in 100% of grafts. (iii) The tumour must grow at a known rate and must never have been known to retrogress spontaneously. (iv) There must be no complication or secondary cause of possible death, such as sepsis, ulceration, interference with a vital function (for example, liver metastases). (v) Carcinoma and sarcoma, both spontaneously arising and chemically induced, must be tested. (vi) All mice must be watched until they die. (vii) All experiments must have untreated controls.

The substance, if it is what we are looking for, will have the following properties: (i) It will not be lethal to the mouse. (ii) It will not give rise to any other disease. (iii) It will stop mitosis in the cancer cells and in no others. (iv) It will do this in both carcinoma and sarcoma, both spontaneous and chemically induced. (v) It will prevent recurrence either of the primary growth or of secondary deposits and the mouse will not die of cancer.

Application of Laboratory Technique to Clinical Trials in Man.

From these considerations it follows that clinical trials of possible cancer cures in man are extremely difficult and fraught with pitfalls for the unwary. Since all the symptoms of cancer in man (apart from the presence of the tumour) are due to the secondary complications of sepsis, pressure, obstruction and hæmorrhage, no improvement in the patients' general condition which does not include disappearance of the tumour can be admitted as evidence of specific action on cancer cells. Many substances, for example, lead (Blair Bell), lead selenide (Todd), bacterial products (Coley and others) and organic compounds of great variety, for example, colchiceine, colchicine, nitrogen mustard *et cetera*, have been used in the past in clinical trials in man. Most of them appeared to produce temporary amelioration, but none has proved of any true value in the treatment of cancer. Early and complete surgical excision still offers the best hope, and in this connexion I must point out that even if a medical means of killing cancer cells specifically should ever be found there will still be immense scope for surgery. Relief of obstruction, mechanical restoration of function, "cosmetic" removal of a tumour mass and control of sepsis will all still be necessary, since cancer in the early stages is not painful and most often presents as an interference with function or as a visible tumour. The scope of a "medical" treatment would be an adjunct to this, to clear up any outlying cells or metastases. Indeed, at the present time patients with advanced inoperable cancer are often temporarily much helped by such means as relieving obstruction by short-circuiting operations, removal of fungating primaries even though metastases are present, and energetic clearing up of secondary infection. All this might still be necessary. It is the presence of such complications and indeed the protean manifestations of the disease which can deceive the most practised investigators, and lead to impressions of improvement in cases in which only the complications have been affected.

Selecting Human Cases for Trials.

Therefore in assessing results of experimental treatment in man the following principles should guide us in picking cases:

1. The disease must have been proved microscopically to be cancer.

2. The tumour must be accessible to measurement (either direct or by radiography or, in leuchæmia, by blood counts).

3. No palliative treatment (for example, X ray, radium, nitrogen mustard, œstrogens *et cetera*) likely to induce temporary improvement should have been used, since any effects observed after the substance on trial may equally well have been due to the preceding palliative treatment.

4. A full evaluation of the part played by sepsis in producing the clinical picture must be made. As far as possible cases without secondary infection should be chosen since many things which it may be advisable to test may also have an action on bacterial infection (for example, X rays).

5. There must be no disturbance of physiological function (for example, obstruction, liver damage *et cetera*) since this will probably kill the patient before the test is complete.

6. The patient must be followed until death and a post-mortem examination performed.

If such or similar stringent rules are observed, clinical trials may run parallel with animal experiment, but it is always the latter which will give us the clear-cut answer. That this is so is seen by the fact that many hundreds of "cancer cures" have been tested in the laboratories of the Imperial Cancer Research Fund and that none of all those which gave a negative result in mice were ever found to benefit a human being. The pressure of public and medical opinion is, however, upon the whole profession, and the exercise of a rigidly scientific approach and an insistence on the slow and meticulous investigations necessary for success demand the utmost strength of mind. Without it, nothing of value will be learned from human experiment, and the "diet of hope deferred" to which we have so long been subjected will be indefinitely prolonged.

THE IMPORTANCE OF THE RELATIVITY OF BLOOD PRESSURE AND OTHER SIGNS IN THE PREVENTION OF ECLAMPSIA.[1]

By T. DIXON HUGHES,

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For many years the value of antenatal care has been questioned by some writers in relation to the prevention of eclampsia, especially the so-called fulminating type. If one examines the standards of antenatal care as laid down by these authors, one cannot help but realize that eclampsia and severe toxæmia will continue to occur so long as such low standards of antenatal care are accepted. It has been noted that eclampsia and severe toxæmia are more prevalent in certain areas than in others, that they are influenced by world affairs, being worse in time of plenty and lessened in war, and that they may vary in incidence from year to year. To avoid the criticism that other factors are respon-

[1] Read at the first Australian conference of Fellows and Members of the Royal College of Obstetricians and Gynæcologists, April, 1951.

sible for the improvement and not the altered standard of antenatal care, Table I is presented. This shows the incidence of eclampsia from 1936 to 1948, and from 1948 to 1951, at the Women's Hospital, Crown Street, Sydney, and the incidence in the two bordering States, Queensland and Victoria, from 1946 to 1950. It will be noted that at the Women's Hospital, among the 48,111 "booked" patients up to 1948, there were 118 who developed eclampsia, an incidence of approximately 1 in 400, and from 1948 to 1951 there were 15,000 patients with five cases of eclampsia, an incidence of 1 in 3000. The incidence in Brisbane is approximately 1 in 517, and that in Melbourne 1 in 320. Therefore, it cannot be argued that in Australia as a whole there has been any material alteration in the rate, or that the condition has vanished because of some national factor since 1948. When we examine the graph in Figure I

TABLE I.

Hospital.	Years.	Number of "Booked" Patients.	Number of Cases of Eclampsia.	Incidence.
Women's Hospital, Sydney.	1936 to 1948	48,111	118	1 in 400
	1948 to present day	15,000	5	1 in 3,000
Women's Hospital, Brisbane.	1946 to 1950	11,898	23	1 in 517
Women's Hospital, Melbourne.	1946 to 1950	23,944	75	1 in 320

we notice that there is a pronounced fall at the Women's Hospital, Crown Street, since 1948—almost spectacular, especially if it is taken into consideration that the only eclamptic seizures recorded in the year 1949-1950 were *post partum*, each of the patients having only one seizure. Furthermore, since March, 1950, to the present time (June 30, 1951), no patient has developed eclampsia among the "booked" patients—a gap of fifteen months and over 6000 consecutive deliveries. Therefore it is fair to assume that some fresh factors must have been brought to bear on this problem. It is these factors that I wish to discuss. It is admitted that no claim to have discovered the cause of toxæmia is made, but the claim is made that its severity can be reduced. Eclampsia is but the summit to which toxæmia inexorably climbs. If the incidence of eclampsia is reduced, we also reduce the stillbirth and neonatal death rate associated with severe toxæmia, and also the permanent injury that remains with some patients after severe toxæmia of any duration. Perhaps the importance of this avenue for prevention of maternal mortality and morbidity is best illustrated by the statement that from 1946 to 1949 36% of all maternal deaths in New South Wales were attributed to albuminuria and eclampsia—by far the largest single cause of maternal death. The fall of the stillbirth and neonatal death rate that has occurred at the same time is mainly due to two facts: (*a*) that the toxæmia rarely reaches a severe degree; (*b*) that induction of labour is not usually called for till the last few weeks of pregnancy.

As the years progressed in my private practice without the occurrence of a case of eclampsia, I became more and more convinced that eclampsia was a preventible condition, and by the time that I had given up private obstetric practice there had been no case of eclampsia in approximately 5000 deliveries. The question arose whether, if this could be achieved in private practice, it could not also be achieved in the hospital amongst those patients who are termed "booked" patients. With the cooperation of the honorary medical staff these standards were introduced into the Women's Hospital. The term "booked" patients means those who have attended the out-patient department once before being admitted to hospital. To achieve success, it is desirable that the patients report early. Our nightmare has been the young *primigravida* who, for some reason or other, is first examined at twenty-four weeks' gestation with what appears to be toxæmia. Her original weight, blood pressure *et cetera* are all uncertain. The results that have been obtained in the abolition of eclampsia are due to the loyal cooperation of the entire staff of the hospital, without whose keenness to succeed nothing would have been achieved. The essential points of a campaign are as follows. (i) Antenatal care must be adequate and must comply with a high standard of efficiency demanding an exacting control of patients, almost personal in nature. (ii) The blood pressure must be properly evaluated. (iii) The weight must be carefully observed and its significance as an indication for treatment, control and closer observation must be appreciated. (iv) Previous ideas of how often a patient should be examined must be scrapped. (v) It must be recognized that the presence of albumin in a catheter specimen of urine is a late sign of toxæmia and that control should commence before its appearance.

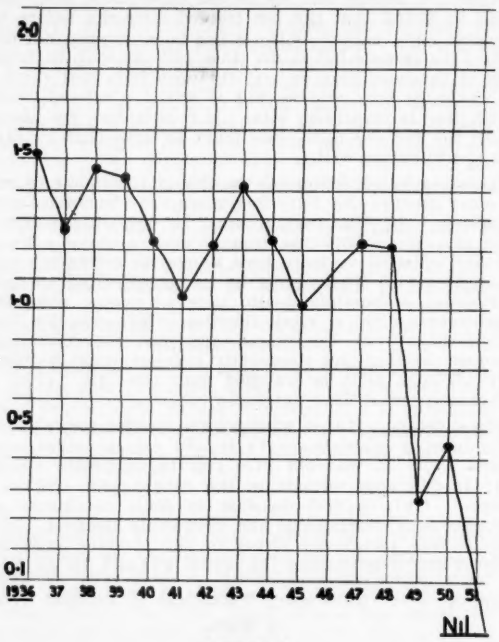

FIGURE I.
Number of eclamptics per 1000 "booked" patients, the Women's Hospital, Crown Street, Sydney.

These points have been put down in what is considered their order of importance, but it is proposed to deal with the second point first—namely, the proper evaluation of blood pressure. To do this the importance of the "relativity of the blood pressure" must be appreciated. What is meant by the term "relativity"? "The Shorter Oxford English Dictionary" defines "relativity" as "the fact or condition of being related to", and when we speak of the relativity of the blood pressure we mean the relationship of the present blood pressure to the blood pressure of that particular patient at the commencement of pregnancy. This is the keystone on which this work is based. We do not lay down a standard of normality of blood pressure or that at which a patient is to be admitted into hospital, because to do so would be to set too low a standard for some and too high a standard for others; whereas, if we judge on a relative basis we shall be more accurate in our interpretation of the status of any particular patient. For example, a patient with a systolic blood pressure of 140 millimetres of mercury on superficial examination may appear to be more seriously ill than one with a systolic pressure of 130 millimetres of mercury; but the latter patient may have had a pressure of 105 millimetres of mercury to start with, so that her systolic pressure has risen 25 points as against 10 points for the former, whose original systolic blood pressure was 130 millimetres of

mercury. One is apt to worry more about the higher figure, whereas the lower figure probably is the potential "atom bomb". If records are examined it is often the young *primigravida* with an initial low blood pressure who provides the majority of the so-called fulminating cases. This idea of the importance of the relativity of the blood pressure is best illustrated by the diagram in Figure II. In the "accepted" idea, patient A would appear to be more advanced than patient B, because we take a common base line at 120 millimetres of mercury, systolic pressure, whereas if we take the base line of each particular patient, the condition is completely reversed. When we lay down a standard of 120 millimetres of mercury, systolic, and 80 millimetres, diastolic, or what you will, we forget the curve of standard deviation, and we should speak of average blood pressure, not the normal blood pressure; so

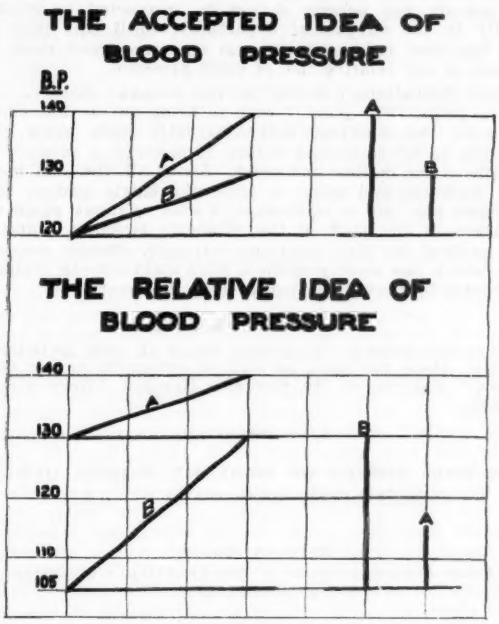

FIGURE II.

let us look at the curve of standard deviation to refresh our minds (Figure III). The normal or average is within the shaded line, so that $\sigma = 10'$ or $-10'$, comprising two-thirds of the population; but we must not forget the group outside the shaded area, representing one-sixth on each side.

From the foregoing accepted facts it must be agreed that to set any standard for all patients is foolish. When considering any alteration of blood pressure, we must estimate the individual rise of blood pressure for each patient—that is, the relation of the present blood pressure for each patient to the original, and not whether it is above or below any artificial standard. Probably variation in the diastolic pressure, when measured by the same observer, is one of the best guides. In this respect I consider a five-point rise a warning for closer observation, and a ten-point rise warrants a review of the patient within seven days. If the rise is accompanied by a rise in weight above one pound per week since the last visit, the patient is suspect, and from then on cannot be allowed away from observation for any length of time. If albumin has also appeared in the urine the patient should be in hospital. On examining my own figures I found that there was no rise in the diastolic blood pressure above 10 points in 75% of my patients. Of the remaining 25%, 20% were admitted to hospital for toxæmia; in other words, 5% of all patients were admitted to hospital, mostly very close to term. In hospital practice this figure is greatly exceeded, owing to the difficulty of controlling diet and obtaining rest and, above all, keeping a careful watch on patients. I have dealt mainly with the diastolic pressure because it appears to be less subject to variation from outside causes, but with discretion the same principle applies to the systolic blood pressure. Whatever you believe, you must judge the rise of blood pressure in the individual patient and consider how many points the pressure has risen from the original figure, and not what is the height of the blood pressure compared with some artificial standard.

Weight.

No measure of antenatal care that disregards weight gain can hope to achieve any great success. In looking

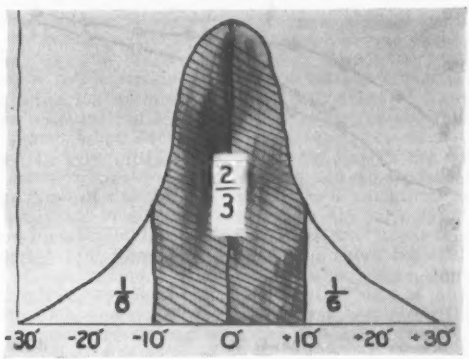

FIGURE III.
Normal curve of standard deviation.

back over the patients who have had 10 points or more rise in the diastolic pressure, one is struck with the sudden gain in weight at one stage in the pregnancy; this usually precedes the rise in blood pressure by weeks, sometimes it is simultaneous, and rarely it is not present. The importance of gain in weight has been questioned by some. This is because some people are concerned with the total gain in weight, which may have no significance, as the patient may have been underweight at the commencement of pregnancy, and although the total gain is large, none of it is sudden and it has mostly occurred in the first three or four months. In my own series the actual average total gain was 26 pounds. This is probably not the true position, as all weights were subject to control. A typical weight graph (Figure IV) shows effective control from twenty-four to twenty-eight weeks; the other graph ("toxæmia") shows ineffective control at this stage with toxæmia developing later. What the average gain would be in an uncontrolled series I cannot say. There can be no question that the weighing machine is a more accurate estimator of hidden œdema than clinical judgement. If the increase is just an increase in fat, then control is none the less indicated, but due regard must be paid to correct diet. Diet plays a part in the control of toxæmia, and hospital patients are often referred to the dietitian for a particular diet; but all patients are given a general talk on this subject by the dietitian. As to the restriction of salt, my own practice is to advise patients not to eat salty foods or to take extra salt, but if there is any undue gain in weight salt restriction is made more absolute and a milk and fruit diet is advised for a day or so. I need not mention the common habit patients have of taking some alkaline powder with bicarbonate of soda to alleviate their heartburn. There is one point that is worth stressing: if a patient has raised blood pressure with increased weight, the weight may be controlled, but the blood pressure may not respond; these patients must be carefully watched, as in them the toxæmia is established. Probably control of the weight acts in two ways: (i) it gives notice of the

development of hidden œdema, (ii) it stops excessive intake of fats and carbohydrates.

In the controlling of the weight common sense must be used, as so many factors are operating in the first five months; but after this any gain above the usual one pound per week must be watched. This may all seem of minor importance, but I quote Sir Bernard Dawson in a personal communication: "I have yet to see a case of eclampsia that did not give warning signs, disregarded, because of their apparent insignificance." This view I most strongly hold.

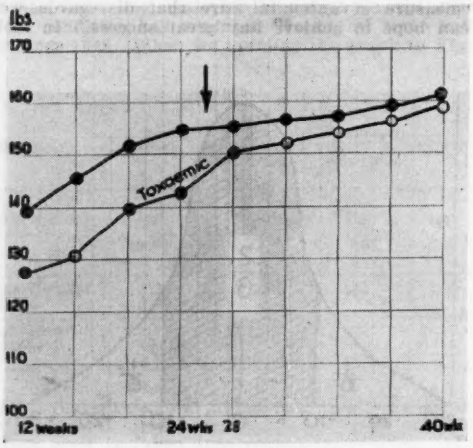

FIGURE IV.
Weight graph.

Albuminuria.

As regards albuminuria, it can be dismissed in a few words. Albumin in a catheter specimen of urine from a previously healthy patient occurring with or without other signs is to be taken as an advanced sign of toxæmia, unless proved otherwise, and in the great majority of cases calls for admission to hospital, particularly if the patient is young. Under the present antenatal *régime* at the Women's Hospital it is almost impossible to find a patient with severe albuminuria for the purpose of teaching.

The Administrative Side.

The administrative side, which is as important as any other aspect, has been very ably carried out by our medical superintendent. An attitude of extreme watchfulness and of fear that one patient may slip through the defences is essential in both private and public practice. The organization must endeavour to arrange by education *et cetera* that patients present themselves within the first three months and, above all, that, when told to report back on a certain day, they do so; if they fail to keep their appointment they must be immediately contacted. This is the responsibility of the organization that looks after the patient, and one cannot offer as an excuse that the patient failed to report. To carry this out means a lot of checking by the out-patient department. Then again, there has to be a checking of all cards of the day's work, to see that the odd stray patient has not gone away without a definite interval appointment corresponding to her condition. This brings us to the question of how often patients have to be examined. In my opinion, once a patient shows any one of the three cardinal signs—increase of weight, rise of five to ten millimetres of mercury in diastolic blood pressure, or albuminuria—she is suspect, and no matter what her stage of pregnancy she should be examined weekly or more frequently till her condition has become stabilized or otherwise. The standards I take are the following. (i) A rise of five points in the diastolic blood pressure means that the patient should be observed within seven days. (ii) If the pressure has increased again within seven days the patient must be either examined in two or three days or admitted to hospital according to the presence or absence of any other signs. The patient's condition can often be stabilized at this stage, provided that a careful watch is maintained, and that her condition does not deteriorate any more. (iii) Albuminuria means admission to hospital. (iv) A weight increase after 20 weeks must be steadied within seven days. Any increase above one pound a week means that the patient must return within seven days to see that she is obeying instructions. If it is impossible to control them out of hospital, irresponsible patients will probably have to be admitted to hospital. (v) Every obstetric patient's out-patient card should be critically examined by the honorary medical officer at the twenty-eighth or thirtieth week, and if the rise in weight during the previous ten weeks has exceeded a total of eight to ten pounds, the patient should be instructed to return weekly to the out-patient department until this rate of gain has been reduced to normal once more and there is no sign of any relative rise of blood pressure.

These indications I should not like to make absolute, but only a guide. The point I wish to bring out is that extra visits at the slightest indication will often allow the toxæmia to be controlled before it becomes a menace to the life of the mother and child. Above all, the staff must have keenness and spirit to enter the battle against this insidious foe. So, in concluding, I wish to thank again all members of the staff of the Women's Hospital, nursing and medical, for their loyal and extremely efficient cooperation, which has made possible a life's ambition—to conquer eclampsia by prevention rather than by treatment.

Addendum.

When the series is taken from March 15, 1950, to October 31, 1951, there has been no case of eclampsia among 6600 "booked" patients at the Women's Hospital, Crown Street, Sydney.

THE IRON LOSSES OF HEALTHY WOMEN DURING CONSECUTIVE MENSTRUAL CYCLES.

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THE various aspects of iron metabolism have been the subjects of many investigations which have been reviewed by Granick (1946), by Laurell (1947) and by Cartwright (1947). However, relatively little is known of the iron losses due to menstrual bleeding, and this study was planned to determine the significance of these losses in a group of healthy women during consecutive menstrual cycles.

The average hæmoglobin level of apparently normal adults has been shown to be significantly higher in the male than in the female (see Table I). The hæmoglobin level in women can be raised to that found in men by the administration of iron salts (Widdowson and McCance, 1936), and this suggests that some degree of anæmia may be present in the "average" woman, rather than that the difference between the sexes is a physiological one. Also there is evidence that there is a higher incidence of anæmia in women than in men; for example, the survey conducted by Davidson *et alii* (1933) on the poor of Aberdeen showed the incidence of anæmia in women to be 46·8%, whereas it was only 11·1% in men.

The level of iron in the body is dependent on the difference between assimilation and excretion. Therefore, the higher degree of iron deficiency found in women may be due to a lower dietary intake of iron, or to less efficient absorption and utilization, or to increased loss of iron from the body as compared with men. Each of these possibilities will be considered in the light of published work and the information obtained from this study. Laurell (1947) finds that the normal level of serum iron

is somewhat higher in men than in women, although the saturation limit is practically the same, and he suggests that either women absorb iron more readily than men or iron is eliminated more rapidly from the blood-stream in men than in women.

By the use of dietary studies, Ohlson and Daum (1935), McCance and Widdowson (1937*a* and 1937*b*), Widdowson and McCance (1942) and other workers have shown that the daily loss of iron in the urine is small and independent of the intake. Barer and Fowler (1937-1938) found the average urinary loss in 100 women was 0·489 milligramme of iron per day, which was 24% higher than the average loss in man (0·395 milligramme). McCance and Widdowson (1938-1939) and Fowler and Barer (1937) introduced iron parenterally and concluded that iron excretion into the colon was negligible. Experiments by means of intravenously administered radioactive iron in laboratory animals confirmed this view (Hahn, Bale, Hetting, Kamen and Whipple, 1939; Greenberg, Copp and Cuthbertson, 1943). Altogether the body excretes approximately one milligramme of iron per day in the urine, bile and intestinal juices, and it is concluded that, unlike most other nutrients, the control of iron stores is through absorption processes rather than by the elimination of excess from the body. Copp and Greenberg (1946) used radioactive iron in their investigations to confirm that the absorption of iron is limited and dependent upon the needs of the body. If iron enters the body in excess of requirements—as, for example, after parenteral administration—it is not excreted but stored in the liver, spleen and bone marrow. Therefore these experiments show that the loss of iron through the bowel and kidneys is small and relatively constant and similar for both sexes.

TABLE I.

The Average Hæmoglobin Value of Apparently Normal Adults.

Male.		Female.		Place.	Reference.
Grammes of Hæmoglobin per 100 Millilitres of Blood.	Number Studied.	Grammes of Hæmoglobin per 100 Millilitres of Blood.	Number Studied.		
14·5	100	13·6	100	London, England.	Price-Jones (1931).
15·8	259	13·8	152	Portland, Oregon, U.S.A.	Osgood (1934).
15·4 to 15·7	4100	13·3 to 13·9	8956	Melbourne, Australia.	Bryce and Jakobowicz (1943).

Otherwise loss of iron from the body occurs as a result of hæmorrhage, and in women there is a periodic loss of blood during menstruation, which may be very significant in determining the requirement for iron. The importance of menstrual loss is also suggested by the observations that the hæmoglobin level up to the age of twelve years is the same in both sexes (Osgood, 1935), and that an appreciable rise in the level in women is recorded in the post-menopausal years, although no significant variation is found in men of a similar age group (Bryce and Jakobowicz, 1943).

The literature on the iron losses in menstruation was reviewed by Frenchmann and Johnston (1949), but such studies are limited in number and often refer to the loss at a single menstrual period. Moreover, the investigations were conducted on women of differing ages, both married and single, and therefore to eliminate some of these variants it was decided to estimate the iron losses during the menstrual periods of a group of healthy unmarried women who were approximately the same age and who had comparable activity. The experiment was planned to follow the losses over several consecutive menstrual periods, to determine whether a significant variation occurred from one period to another. The hæmoglobin levels in blood were recorded each week in order to detect any alteration in the level during the menstrual cycle. In addition, a dietary record was kept during part of the experiment to ascertain whether the diet supplied to the subjects of the investigation would contain sufficient iron to replace the loss.

Methods.

Fourteen third-year nursing trainees at the Royal Melbourne Hospital volunteered for the study. These students lived in the nurses' home and were aged twenty-one to twenty-seven years. They performed their normal work, which includes forty-four hours on duty in different wards, attendance at lectures and additional study in their free time. A small and variable number of the nurses were on night duty for part of the study period, but some of the subjects were not required for night duty at any time during the investigation.

Each subject was given a thorough medical examination at the beginning of the experiment and was checked each week, when a sample of capillary blood was withdrawn from a finger for hæmoglobin estimation. The errors in the collection of blood and the estimation of hæmoglobin have been fully discussed in the report of the Committee on Hæmoglobin Surveys to the Medical Research Council, Great Britain (1945). In this investigation the collection of samples was made each week at approximately the same time of day to eliminate diurnal variations as much as possible. The estimations were all performed by the same member of the medical staff of the Royal Melbourne Hospital (Dr. Dorothy Chong), and therefore the figures are of comparable if not absolute value. Hæmoglobin was determined as acid hæmatin by the use of the Sahli hæmoglobinometer, 100% hæmoglobin being equivalent to 14 grammes of hæmoglobin per 100 millilitres of blood. This method was selected as it is the one commonly used by medical practitioners in Melbourne and the figures would indicate the degree of variation in hæmoglobin level which might be expected in general practice.

The menstrual flow was collected on cotton pads, which were then digested in sulphuric acid (10% to 15%) for ten to fourteen days in an oven at 70° C., as in the method of Leverton and Roberts (1937). The digests were considered ready for ashing when the slurry was uniform in colour and consistency. Aliquots were ashed in silica crucibles in a furnace at 400° to 430° C., and the ash was extracted with concentrated hydrochloric acid as described by McCance and Shipp (1933). The iron was determined in aliquots of the extract by the thiocyanate method of Stugart (1931). Blank determinations were performed on the pads and reagents, and allowance was made in the calculation of results.

The dietary department of the Royal Melbourne Hospital kindly supplied the records of food consumption from which iron intake was calculated. These records were based on the amount of food prepared and served in the main kitchen and the number of persons who received meals in the nurses' dining room. The average serving per person was calculated and the iron content of the diet was then assessed from tables (Tables of the Composition of Australian Foods, 1948). As stainless steel equipment is used in the kitchen, the addition of iron during food preparation would be small. It was considered that a period of two weeks would give a sufficiently accurate measure of the food intake in the hospital dietary. No allowance was made for plate waste, and it is realized that the intake figures will be inaccurate for a particular individual, as no records were kept of food consumed away from the dining room.

Results and Discussion.

The percentage of hæmoglobin in blood in each subject varied from week to week, but there is no consistent relationship between hæmoglobin levels and the duration of the menstrual cycle (see Table II). The menstrual loss of subject VI was the lowest for the series, and it seems unlikely that this is the causative factor for the low levels of hæmoglobin recorded for this person. The

TABLE II.

Date (1950).	Hæmoglobin Value (Percentage) of Subject.[1]													
	I.	II.	III.	IV.	V.	VI.	VII.	VIII.	IX.	X.	XI.	XII.	XIII.	XIV.
April 12	100 (April 14 to 16)	85 (April 17 to 22)	90	100	88	78	95	95	90	95	85	78	100	95
April 19	85	85	92 (April 24 to 28)	83	89	75	97	97	95	89	84	75	100	90
April 26	90	93	90	78 (April 28 to May 2)	80 (April 27 to 30)	88 (April 27 to 30)	93 (April 27 to May 1)	90	90 (April 30 to May 5)	100	83	90	93	95
May 3	94	100	90	85	83	86	100	—	83	90 (May 3 to 8)	88	90	94	—
May 10	88 (May 10 to 14)	90 (May 14 to 19)	94	86	90	86	95	100 (May 4 to 7)	95	90	— (May 11 to 14)	87	100	—
May 17	85	100	95	96	90 (May 23 to 26)	84	95	—	95	87	95	90 (May 17 to 21)	97 (May 18 to 23)	97
May 24	95	90	85 (May 25 to 29)	90 (May 28 June 1)	75	84	85 (May 24 to 29)	95 (May 28 to 30)	90 (May 28 to June 2)	92	—	75	100	83 (May 25 to 30)
May 31	90 (June 2 to 6)	87	85	90	85	90 (May 31 to June 3)	—	—	91	89 (June 3 to 9)	90	75	100	90
June 7	78	97 (June 7 to 12)	85	90	80	85	91	85	80	95	80 (June 4 to 7)	75	89	95
June 14	100	86	85	85	78 (June 20 to 23)	—	95	100	88	90	83	70 (June 15 to 23)	85	100 (June 20 to 25)
June 21	82	90	80 (June 21 to 26)	90 (June 22 to 25)	84	73	98	95	96	82 (June 27 to July 2)	85	82	88 (June 24 to 28)	96
June 28	91 (June 30 to July 4)	95 (July 4 to 10)	87	95	88	85	90 (June 28 to July 2)	95	95 (June 30 to July 5)	100	90 (July 2 to 5)	82	85	100
July 5	90	85	87	88	82	78	90	85	—	95	85	78	85	90
July 12	85	90	93	80	— (July 17 to 20)	78 (July 16 to 19)	90 (July 18 to 23)	95	83	86	88	75	95	95 (July 12 to 17)
July 19	— (July 22 to 27)	90 (July 25 to 31)	82 (July 19 to 24)	85 (July 24 to 27)	84	80	95	90 (July 23 to 26)	92	95	88	80 (July 19 to 23)	90	93
July 26	85	90	92	90	90	78	85	100	— (July 30 to August 5)	90 (July 26 to August 1)	90	100	90 (July 28 to August 1)	92
August 2	90	95	90	80	78	88	92	—	—	86	90 (August 2 to 5)	90	100	88 (August 4 to 9)
August 9	—	93	85	91	95 (August 14 to 18)	85	85	—	87	—	92	85	—	—

[1] Menstrual periods shown in parentheses. A hæmoglobin value of 100% is equivalent to 14 grammes of hæmoglobin per 100 millilitres of blood.

administration of ferric ammonium citrate resulted in an increase of percentage of hæmoglobin in blood to 90%, indicating that this subject was in a state of iron deficiency. The percentage of hæmoglobin in blood may not be a satisfactory indication that the iron stores in the body are being maintained. There was no pronounced change in the levels during the period of study, but the effect of a slow depletion of iron reserves would not be obvious unless the study was prolonged over a number of years.

The duration of the menstrual cycle varied in different subjects and also in the same subject. Arey (1939) reported for 585 persons an average duration of 28·4 days for women aged over nineteen years, but the range varied from 11 to over 100 days. In the present series the range was from 21 to 55 days, with an average of 28·7 days. The duration of the menstrual period was between three and seven days, but there is no correlation between the amount of iron lost and the duration of the menstrual period or cycle.

It will be seen from Table III that the loss of iron varied from one subject to another, within the limits of 3·5 and 66·8 milligrammes of iron per menstrual period, and the average for 57 menstrual periods was 21·8 milligrammes. It was apparent from questioning that all the nurses considered they had normal menstrual periods and that they had no idea whether their losses were greater or smaller than the average—that is, they had no standard for comparison. In some cases—for example, subjects II, X and XIII—there was considerable variation in the amount of material lost during different menses, but this was not detected by the subject. It will be observed that the number of sanitary pads required to collect the menstrual flow is not a guide to the degree of loss, but is largely a personal matter. In 1936 Barer and Fowler reported the menstrual losses of 100 normal women aged between fifteen and forty-three years, and in all except 13 cases the determinations were made on the loss at only one menstrual period. They found that although the losses varied from 2·28 to 78·96 milligrammes of iron, 58% of the cases fell within the range of 5·8 to 22·6 milligrammes, and in this series 65% of the cases lie within this arbitrarily selected range.

Leverton and Roberts (1937) found for four college women the amount of iron lost in different menstrual periods was constant for the same subject, whereas Schlaphoff and Johnston (1949) reported that six adolescent girls showed considerable variation in the loss in different menstrual periods. In the study recorded in this paper the alteration in loss of iron in some subjects was more significant than in others, and for a number of the subjects the loss is remarkably constant. Unless the variation is small, estimations on the basis of one or two consecutive menstrual periods will be misleading, and in general larger differences were recorded for subjects whose losses were higher than the mean for the group. It can be seen from Table III that the variability within the series was much greater than that of any subject except for subject XIII. Five observations were made on this subject and showed wide differences in the amount of iron lost

TABLE III.

Subject.	Age (in Years).	Iron Loss. (Milligrammes.)[1]	Variability. (Standard Deviation).	Duration of Menstrual Period. (Days.)	Duration of Menstrual Cycle. (Days.)	Number of Pads Used.	Replacement Iron Required. (Milligrammes per Day.)
I	21	(i) 10·2 (ii) 10·6 (iii) 12·2 (iv) 19·3 (v) 15·5 Mean 13·6	±3·9	5 5 5 6 6 5·2	26 23 28 22 25	8 9 9 11 9	0·55
II	22	(i) 36·8 (ii) 49·7 (iii) 59·6 (iv) 55·8 (v) 42·0 Mean 54·8	±9·4	6 6 6 7 7 6·4	27 24 27 21 25	10 14 15 9 10	2·20
III	21	(i) 21·3 (ii) 21·0 (iii) 19·0 (iv) 21·5 Mean 21·0	±1·2	5 5 5 5 5	31 28 28 29	11 10 9 9	0·72
IV	21	(i) 31·7 (ii) 27·8 (iii) 32·1 (iv) 32·4 Mean 31·0	±2·5	5 5 4 4 4·5	30 25 32 29	24 20 18 16	1·06
V	21	(i) 9·7 (ii) 12·4 (iii) 15·2 (iv) 12·6 (v) 10·3 Mean 12·0	±2·2	4 4 4 4 5 4·2	27 28 27 28 27·5	9 10 14 14 8	0·46
VI	22	(i) 3·5 (ii) 3·2 (iii) 8·8 Mean 5·2	±3·2	4 4 4 4	34 46 40	8 11 9	0·12
VII	21	(i) 11·5 (ii) 11·3 (iii) 13·1 (iv) 17·6 Mean 13·3	±2·8	5 6 5 6 5·5	27 35 20 27·3	8 7 8 8	0·47
VIII	21	(i) 5·9 (ii) 6·2 (iii) 7·3 Mean 6·5	±0·7	4 3 4 3·6	24 55 39·5	6 7 8	0·15
IX	21	(i) 31·2 (ii) 20·2 (iii) 17·5 (iv) 16·7 Mean 21·4	±6·7	6 5 6 7 6	28 32 31 30·6	10 8 7 9	0·67
X	21	(i) 24·8 (ii) 35·6 (iii) 18·0 (iv) 35·0 Mean 28·4	±8·5	6 7 6 7 6·5	31 24 29 28	16 18 16 16	1·00
XI	22	(i) 13·4 (ii) 10·2 (iii) 14·7 (iv) 9·5 Mean 11·9	±2·5	4 4 4 4 4	24 28 31 27·6	8 9 11 12	0·44
XII	21	(i) 17·3 (ii) 18·6 (iii) 16·3 Mean 17·4	±0·1	5 6 5 5·3	29 34 31·5	15 13 15	0·56
XIII	21	(i) 60·8 (ii) 46·0 (iii) 23·4 (iv) 33·0 (v) 37·4 Mean 40·1	±14·1	6 5 5 5 5 5·2	37 34 30 30 32·8	18 13 12	1·22
XIV	27	(i) 9·7 (ii) 15·5 (iii) 13·1 (iv) 8·6 Mean 11·7	±3·2	6 6 6 6 6	26 22 22 23·6	10 11 12 7	0·53
Average for 57 menstrual periods ..	21·8		±15·0[2] ±13·9[3]	5·1	28·7	11·3	

[1] In successive menstrual periods.
[2] Standard deviation of mean of means of each subject.
[3] Standard deviation of mean of all readings.

per menstrual period; but an inquiry into the medical history and careful checking of experimental details failed to explain the variability.

The importance of the elimination of iron in the menstrual flow is dependent not only on the amount excreted at each menstrual period, but also on the duration of the

cycle, as this will determine the average replacement per day which will be required if the subject is to maintain a state of equilibrium with respect to iron.

The iron intake was dependent on the selection of foods provided in the menu and therefore was not constant from day to day. The average intake of iron for fourteen days was 12·60 milligrammes (range 10·04 to 20·09 milligrammes), which is slightly above the American National Research Council recommendation (1948) of 12 milligrammes of iron per day. McCance and Widdowson (1942) found an average absorption of 12·5% iron intake when half the Calories were derived from white flour and the remainder from a mixed diet; but the absorption of iron was much lower when the white flour was replaced by 92% extraction flour, owing to the formation of insoluble ferric phosphate. In this experiment only a small proportion of the cereal eaten was in the form of wholemeal, and the consumption of 600 millilitres of liquid milk per person would provide a calcium : phosphorus ratio likely to aid the absorption of iron. Johnston, Frenchmann and Boroughs (1948) found that 11% of iron was absorbed from a normal mixed diet containing seven milligrammes of iron, but the absorption increased to 21%—that is, 2·18 milligrammes—when the intake of iron was raised to 10·4 milligrammes by the addition of beef.

Four of the 14 persons studied require one milligramme or more of iron per day to replace the loss in menstrual fluid. Therefore at least two milligrammes of iron would have to be absorbed each day to replace the losses in urine, fæces, bile and menstrual fluid, and this represents an absorption of about 16% of the recommended iron intake.

Dubach, Callender and Moore (1948) investigated the absorption of radioactive iron by normal men and women, and reported that it occasionally exceeds 10%. However, it should be remembered that the error in the assay of Fe_{59} in fæces is large, and therefore the results obtained by such methods should be accepted with reserve.

Balfour, Hahn, Bale, Pommercuke and Whipple (1942), in studies of absorption of radioactive iron, found that when there is a need in the body for iron, as in pregnancy and iron deficiency states, the iron intake is increased above normal. Pregnant women with no anæmia absorbed 16% to 27% of the iron intake, which is two to ten times the "normal" absorption of radioactive iron. In their experiment as much as 100 milligrammes of iron were given orally, and Laurell (1947) points out that a considerable rise in serum iron content after the ingestion of a large dose of iron does not signify that the subject under physiological conditions is able to utilize the iron in his food.

Bale, Hahn, Ross, Balfour and Whipple (1943) studied the absorption of radioactive iron in dogs after acute loss of blood. The absorption in normal dogs was 1·2% of the iron intake, and that in dogs rendered anæmic by hæmorrhage 10·4% to 13·6%; the dogs therefore absorbed ten times more iron after being bled. Further investigations are required to show if the human being behaves in a similar way.

On the basis of information available at present, women who have to replace iron from menstrual loss at the rate of less than one milligramme per day can do so if they ingest an adequate diet. However, further studies in the absorption of iron under physiological conditions are required to show whether larger amounts of iron can be absorbed. A certain number of women in the group studied in this investigation have higher losses, and in the case of Subject II it is necessary to have an absorption of more than three milligrammes of iron per day to replace all losses from the body—that is, at least 25% of the ingested iron—if the diet attained the recommended intake of 12 milligrammes. Therefore a number of healthy women are situated unfavourably for the maintenance of iron equilibrium, and in these women it seems likely that a gradual depletion of the iron stores in the body will occur and may eventually be reflected in the hæmoglobin level in the blood.

Summary.

The iron losses were determined during consecutive menstrual periods in a group of 14 normal healthy young women, and a pronounced individual variation was shown. The average loss was 21·8 milligrammes of iron (range 3·2 to 66·8 milligrammes).

The iron losses in a subject varied from one menstrual period to another, and therefore it is necessary to determine the losses on more than two occasions to obtain a reliable figure.

The average duration of the cycle was 28·7 days (range 21 to 55 days).

The significance of the menstrual loss in the maintenance of iron balance in women is discussed.

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Reviews.

PROTHROMBIN DEFICIENCY.

IN "Prothrombin Deficiency" Rosemary Biggs gives a brief but clear and critical analysis of the theories and experimental work underlying the methods of estimation of prothrombin,[1] dating from the work of Quick and many others since 1935 onwards. This work has necessitated revision of our earlier relatively simple conception of blood coagulation, and while greatly increasing our knowledge and the scope of investigation possible, has, as is so often the case, also brought in its train a great diversity and intensity in subsequent investigations, which to those attempting to follow their implications are sometimes difficult to evaluate and to coordinate.

A survey such as is provided with such clarity in this little book is therefore both timely and welcome. Clinical pathologists, and others concerned with the performance and interpretation of tests for prothrombin activity, whether for diagnosis of abnormalities of coagulation, or for control of anticoagulant therapy, will also appreciate the detailed descriptions of various technical procedures, and the discussion of their value and limitations, the more so since they are the result of the personal practical experience of a member of the department of hæmatology at the Radcliffe Infirmary, Oxford, so well known for its constructive and well-balanced work in this field.

HANDBOOK OF PSYCHOLOGY.

DR. J. H. EWEN'S neat and tidy little book is called a "Handbook of Psychology", and it is rightly named.[2] It is certainly not a "Text-Book of Psychology". It does not become ponderous with the heaping up of example upon example of psychological cases as does a text-book whose author is anxious to illustrate freely every principle advanced. Dr. Ewen does not illustrate at all: he assumes the reader is familiar with cases, but wants to know about procedures.

Another of the book's virtues is the complete absence of jargon, joined with a notable economy of word and statement. The author's method is at once to define succinctly and forthwith to develop the implications of the definition with the same economy of word and statement. Indeed, the neatness and clarity of exposition are notable features of the whole book. To exemplify the author's consistent method and style one may cite his exposition of conation (page 21):

> Conation is the felt capacity for striving. All willing, wishing, craving and desiring are conative impulses seeking satisfaction. It will be noted that conation is a felt capacity and therefore conation and its fulfilment cannot coincide in the same moment of consciousness since the conative impulse would be merged in its goal and would not be felt. Hence full satisfaction is delayed and may come by gradations each giving partial satisfaction only. In the operation of the so-called instinct of curiosity which, in reality, is an attitude of suspended judgement, full satisfaction may be impossible to achieve as in metaphysical speculations since the means of satisfying curiosity may not be available.
>
> Conative impulses are characterized by great strength and continued persistence, but may die of fatigue, disappointment, or inability to reach their goal, although conation may persist subconsciously and influence conscious behaviour. In the well-integrated mind conation persists over very long periods and the operation of conative trends are of considerable importance in the evolution of personality.

There we have, once and for all, the basis of human striving, with its elation at success and its depression at failure of attaining its object.

Again, turning to the life of feeling and emotion we have the following (pages 24 and 25):

> Affection is feeling tone and is the consciousness of what is happening within the organism . . . one of the modes of being conscious of an object is the feeling-attitude or affection. Whatever furthers the conative impulse gives a feeling-tone of pleasure, whatever hinders conation in the achievement of its aim yields a feeling attitude of pain. The term hedonic tone is used in the description of the relationships between conation and affection and it denotes the pleasure or pain involved in a mental process.
>
> When an organism is stimulated the consciousness that the organism has of the stimulus is the affect, affection, or feeling. A state of feeling is the most basic perceptible state of consciousness and it serves as an indicator of the effects of the environment upon the organism. No special sense organ is concerned in affection which is a vague feeling tone which pervades mental processes and, although it has quality, intensity and duration, it is not localized nor has it definite form.
>
> Further variations of feeling attitude are found in the emotions and sentiments, but in the emotions the feeling tone is specific and distinct from the hedonic tone, while in the sentiments there is an organized system of emotional tendencies.

The author's method is one of continuous defining, so clear and well informed that it is most effective. He confronts each difficulty as it arises. He also informs the reader clearly and succinctly of the position taken up by the various schools.

The contents of the book are divided for treatment into two sections. Section I: Normal psychology which includes intelligence; sleep and dreaming; the unconscious mind; behaviour and *Gestalt*. Section II: Treating of psychology and psychiatry and including mental mechanisms, delusions, hallucinations, and illusions; mental disorder; psychoanalysis, psychology and mental treatments in mental disorders.

The book is to be commended for its clarity of exposition and its sanity. Its value would grow with the use one made of it.

[1] "Prothrombin Deficiency", by Rosemary Biggs, M.D.; 1951. Oxford: Blackwell Scientific Publications. 9″ × 5½″, pp. 92, with 14 text figures. Price: 10s. 6d.

[2] "Handbook of Psychology", by John H. Ewen, F.R.C.P.E., D.P.M.; 1950. London: Sylviro Publications, Limited. 7¼″ × 5″, pp. 216. Price: 25s.

Notes on Books, Current Journals and New Appliances.

CURRENT MEDICINE.

WHILE not intended to be exhaustive in the material it presents, "Medicine of the Year" for 1951 presents a useful summary of current medical knowledge.[1] It consists of a series of articles, 18 in all, by leading medical practitioners in the United States; the author of each particular article recounts, explains and assesses contributions made to his subject in the year. The aim appears to be to provide

[1] "Medicine of the Year", edited by John B. Youmans, M.D.; Third Issue; 1951. Philadelphia: J. B. Lippincott Company. Sydney: Angus and Robertson, Limited. 9½″ × 6¼″, pp. 304. Price: 53s. 9d.

information of mainly clinical interest which will be helpful to the doctor in active practice. The volume should be a useful addition to the considerable number of annual publications now appearing which seek to present the gist of current medical developments.

EXERCISES AFTER CHILDBIRTH.

As a contribution to the well-being and restoration to normal health of mothers after childbirth, Gertrude Behn's little book "Exercises after Childbirth" may be commended.[1] The author's aim has been to explain simply with the aid of photographs and sketches a course of exercises to be performed for six weeks from the first day of delivery. The aims of the exercises are to strengthen muscles, particularly those stretched during pregnancy or labour, to reduce excessive fat, to maintain the firm shape of the breasts and secure an adequate milk supply, to correct posture, and to restore the mother's morale and foster a confident attitude of mind. The book is written in terms that should be readily understood by any reasonably intelligent woman, but it should also be acceptable to medical practitioners and others who have the care of the mother during the puerperium. In a foreword, Linton Snaith, senior obstetrician and gynæcologist at the Newcastle General Hospital, states that the exercises described have been in use in the Department of Obstetrics in Newcastle General Hospital for the past six years, and that everyone concerned with the care of the patients in that department has been convinced of their value in restoring health and confidence in the women confined there.

NOTES ON GENETICS.

THE object of "Introductory Courses in Genetics", by Charlotte Auerbach, is to help students who attend courses in elementary genetics, especially the short courses given to medical students and first-year agricultural students, for whose special requirements two appendices have been added.[2] The author considers that the notes should relieve the student of the necessity to take his own notes on a subject which requires great accuracy and clarity of terminology. The book has, in fact, grown out of dictation to students and has successfully replaced this dictation in the introductory courses given by the author, who is a member of the staff of the Institute of Animal Genetics in the University of Edinburgh. She states that the book is not intended to compete with any text-book, however elementary, and even less to be a popular introduction to genetics, although it is thought that it may prove useful to scientists in other branches who want a concise exposition of the basic concepts and laws of genetics. The book consists mostly of concise, simple sentences of an essentially dogmatic character. The subject matter is concentrated, and the number of words is reduced to a minimum. Teachers of genetics might care to examine it for what it is intended to be—a means of providing students with accurate notes on essentials, so that they may devote their attention to the lecture itself.

"THE CRY AND THE COVENANT."

THIS book tells the story of the Hungarian Ignaz Semmelweis, and his work on puerperal fever.[3] In spite of a rather trying style of staccato, journalistic writing in parts, the book is interesting because of the vivid picture it gives of the medical profession generally in the middle of last century, and in particular in Vienna and Budapest. No detail is overlooked, and the reader is dragged remorselessly through the lecture room, the operating room, the hospital ward and the autopsy room. Not the least interesting feature is the picture of intrigue and political manœuvring which lay at the back of medical appointments in those days.

The way of the innovator was hard indeed, and Semmelweis fought a lifelong battle—against professors who objected to answering awkward questions from students, against the crippling animosity of superiors who abhorred innovations and the originators of them, against the sullen hostility of students and nursing staff who thought it an indignity to wash their hands before examining patients, against filth and smells and apathy and poverty. He died by his own hand finally, broken in mind by a lifetime of disappointment and ceaseless struggle. The aim of his life, the prevention of suffering and death by the use of a few simple rules of cleanliness, was realized only after many years. The book ends with Lord Lister's words: "Without Semmelweis my achievements would be nothing. To this great son of Hungary Surgery owes most."

[1] "Exercises after Childbirth", by Gertrude Behn, M.C.P.S., with a foreword by Linton Snaith, M.D., M.S., F.R.C.S., F.R.C.O.G.; 1951. Edinburgh: E. and S. Livingstone, Limited. 9" × 6", pp. 32, with 36 illustrations. Price: 3s.

[2] "Notes for Introductory Courses in Genetics", by Charlotte Auerbach, Ph.D., D.Sc.; Third Edition; 1951. Edinburgh: Oliver and Boyd. 7½" × 5", pp. 42. Price: 2s.

[3] "The Cry and the Covenant", by Morton Thompson; 1951. London: William Heinemann (Medical Books), Limited. 8" × 5½", pp. 502. Price: 18s. 9d.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Surgical Care: A Practical Physiologic Guide", by Robert Elman, M.D., F.A.C.S.; 1951. New York: Appleton-Century-Crofts, Incorporated. 10" × 7", pp. 604, with about 60 illustrations and text figures.

The author seeks "to outline a positive program of surgical convalescence or care that differs considerably from the traditional policy of 'letting nature take its course'".

"The Practice of Endocrinology", edited by Raymond Greene, M.A., D.M., M.R.C.P.; Second Edition; 1951. London: Eyre and Spottiswoode. 10" × 6½", pp. 412, with 56 plates and 25 text figures. Price: 65s.

One of "The Practitioner Series", intended for the general practitioner. The first edition appeared in 1948.

"Muir's Text-Book of Pathology", revised by D. F. Cappell, M.D., F.R.F.P.S.G.; Sixth Edition; 1951. London: Edward Arnold and Company. 9" × 6", pp. 1110, with 636 illustrations. Price: 50s.

The first edition was published in 1924; the fifth, which appeared in 1941, was twice reprinted.

"Alice and the Stork: Or the Rise in the Status of the Midwife as Exemplified in the Life of Alice Gregory, 1867-1944", by Egbert Morland; 1951. London: Hodder and Stoughton, Limited. 8" × 5½", pp. 88, with 14 illustrations. Price: 7s. 6d.

Alice Gregory was a pioneer in maternal and infant welfare work; this is her story. The author was for some years editor of *The Lancet*.

"Medical Disorders of the Locomotor System Including the Rheumatic Diseases", by Ernest Fletcher, M.A., M.D. (Cantab.), M.R.C.P.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 10" × 6½", pp. 896, with 377 illustrations. Price: 60s.

The second edition of a work first published in 1947 with the object of bringing under one cover the available information on medical locomotor disorders.

"The 1951 Year Book of Pediatrics (July, 1950-June, 1951)", edited by Henry G. Poncher, M.D., with the collaboration of Julius B. Richmond, M.D., and Isaac A. Abt, M.D.; 1951. Chicago: The Year Book Publishers, Incorporated. 8" × 5½", pp. 442, with 98 illustrations. Price: $5.00.

One of the Practical Medicine Series of Year Books.

The Medical Journal of Australia

SATURDAY, DECEMBER 29, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

SKILL AND AGE.

IT has been said that all things require skill but an appetite. While one might not wish to argue the truth of this statement, one can imagine that the subject of anorexia must often wish for some skill of his own to make him desire food—the skill of his doctor may give him what he needs, but that is different. If we ask for a definition of skill we find that the Oxford Dictionary refers to "capability of accomplishing something with precision and certainty" and to "practical knowledge in combination with ability". Though the saying about skill and appetite would imply that practically everyone had skill of sorts, the Oxford Dictionary suggests that a man must have a certain endowment or quality before he can display it. Most people have enough skill to earn a living, and, though it is somewhat beside the point, there are those who with the greatest skill contrive to get a living without earning it. Many people go on earning a living until they are quite old, and it would be of the greatest interest to inquire into the possible changes in quality, intensity or direction of their skill with the passage of the years. Custom has decreed that men and women in certain occupations shall "retire" when they have attained a stated age. Many of them are still able to work and with skill. This is true also of some who qualify for and receive old-age pensions. The earning capacity of these people and its importance in the social economy have been referred to from time to time in these columns and the appearance of a book entitled "Skill and Age" has prompted further reference to it.[1]

The book is the report of an experimental investigation for the Nuffield Foundation by members of a Nuffield Research Unit at the Psychological Laboratory, Cambridge. The book is by A. T. Welford, who has had a team of eight assistants. In a foreword Professor Sir F. C. Bartlett points out that heretofore investigations of the effects of aging on human performance have been characterized by three things. In the first place the principal preoccupation has been with the behaviour of the relatively elderly. Secondly, more attention has been given to the disabilities of aging than to any of its possible advantages. Thirdly, nearly all measures considered have been measures of simple bodily or mental functions carried out in isolation from all others. The experimental approach adopted by Welford and his associates is different. It is not much concerned with behaviour in extreme old age, but treats aging as a more or less continuous process and is just as much concerned with the discovery of what older people can do better as with finding what they usually do worse. Clearly this direct method has a great deal to commend it. For this kind of study it is necessary to have a clear conception of the nature of skill. A chapter is devoted to this subject; it is not easy to read and the meaning has to be disentangled from an over-generous use of words. In regard to the mechanisms of skilled activity the author refers to a chain of processes as being in two parts. There are the "receptor" processes which have to do with the interpretation of an incoming stimulus and there are "effector" processes which shape the resulting action. In the light of these ideas, performance which can be termed skilled has three characteristics. The first is that the performance is "the building of an organized and coordinated activity in relation to an object or display" and involves the whole receptor-effector chain. The second characteristic is that the performance is learned "in that the understanding of the display and the form of the action are built up gradually in the course of repeated experience". Thirdly, the performance is "serial and dynamic" because of the constant interplay between the receptor and effector functions and *vice versa*. On the receptor side stimuli undergo a process of organization before they reach the stage of perception, and in this process selection of data takes place, some being relegated to the background and others chosen as dominant and all-important. Past experience takes a prominent part in the process of organization. In regard to the learning of a skilled performance it is pointed out that as this becomes more nearly complete there tends to be a dropping out of conscious control and possibly of some of the stages in the receptor and effector processes; this results in economy of effort. For the study of aging the learned aspect of skill is held to be specially important—"while older people seem less capable than younger of building up new skills, they can often carry on with a high degree of efficiency a skill already learnt". We do not propose to describe the experiments carried out in this investigation, suffice it to state that they had to do with manipulatory and mental skills. Every experiment showed changes associated with age which did not appear to be due to deterioration of peripheral mechanisms—sense organs or muscles. These changes "were rather to be located within the central mechanism of the brain concerned with the organization of incoming data and outgoing action". This means that the changes were rather on the receptor than on the effector side. Even when change of performance was noted it appeared strongly probable that receptor functions were to some extent responsible. This suggests, we are told, the possibility

[1] "Skill and Age: An Experimental Approach", by A. T. Welford and members of the Nuffield Research Unit into Problems of Ageing at the Psychological Laboratory, Cambridge, with a foreword by Professor Sir Frederic C. Bartlett, C.B.E., F.R.S.; 1951. London: Geoffrey Cumberlege, Oxford University Press. Melbourne: Oxford University Press. 9" x 6", pp. 170, with nine figures. Price: 16s.

that in normal skilled activity effector mechanisms set limits less often than is commonly supposed. When the capability of a subject is impaired, this change will not in general lead to a commensurate fall in achievement. What happens is that the method is changed and that possibly effort has to be increased.

At the outset of this discussion reference was made to the ability of many persons to work when they are supposed to retire. The experiments of Welford and his collaborators have at least in theory a bearing on this subject. If we can discover at what particular point in a chain of events resulting in a skilled action the failure due to age is likely to occur, we may be able to arrange the life of the individual in such a way that he will not be compelled to "retire" from work. Welford did undertake some studies in industry. A number of factories were visited and operations were investigated; those chosen were likely to be of psychological interest or were carried out by an unusually high or an unusually low proportion of older people. Welford insists that these studies were preliminary only, and that any inferences based on them must be tentative. One important point noted was that older people tended to be found doing work in connexion with which there was an absence of time stress—"work which could be done at their own pace, unhurried by pressure for speed, and where there was opportunity for accuracy to be displayed to advantage". In some occupations a man using a machine has to keep up with mechanical speed; for the rest we may say that provided a man is healthy in mind and body and wants to work, he will do his best work at his own pace and unhurried by pressure for speed. An aging person may find it difficult to acquire a new skill; his ability to do this will depend to some extent on the range of his activities—work and hobbies—throughout his life. If through the years he has done one thing and one thing only—the thing being his single job of work—it will be hopeless to ask him to acquire skill at something new when his age makes his single job of work unsuitable for him. Health, personality and temperament as well as environment all have to be considered in the planning of work for aging men and women. Generally speaking common sense with understanding will solve most difficulties. Experimental tests for the working capacity of older people will be useful in the future when work of the kind described by Welford is extended and put on a practical basis. But like intelligence tests for growing boys and girls, they will tell only part of the story. Another aspect of this big subject, and one which will have to be considered before long, is the dovetailing into the social economy of a plan for work by old persons so that, on the one hand, there shall be no interference with normal everyday work, and on the other, old people will not be exploited, as they often are. This aspect merits the attention of the trades union organization.

Current Comment.

THE HEALTH OF FERROUS FOUNDRYMEN.

THE latest available figures reveal that there are approximately 341,000 production workers employed in ferrous foundries in the United States of America. They are engaged in the manufacture of iron or steel castings, in which the principal steps are as follows: the preparation of moulding materials, the making of moulds and cores, the making and pouring of hot metal, the removal of castings from the moulds and the removal of cores, and the cleaning of castings. A detailed examination of these operations indicates that the major health hazards to workers are exposure to silica dust, iron dust, carbon monoxide and aldehydes, and to such physical agents as heat, rapid changes in temperature, noise and bad illumination. Possibly the most important of these is exposure to silica dust. Silicosis, as it occurs in various industries, has received much attention of recent years, and a good deal has been done to lessen or even to eliminate it as a hazard. It has certainly not been neglected in the foundry industry, but the progress made has not been considered entirely satisfactory. Officials from certain mid-western States drew attention to the continuance of claims for silicosis among workers in the ferrous foundry industry, in spite of apparent improvement of environmental conditions, and at their request a special investigation has been made of the health of workers in the industry. It was agreed to carry out the investigation in the State of Illinois, and for this purpose 18 foundries, which were considered representative of the 185 foundries in the State, were selected for special study. The report of this investigation by the Division of Industrial Hygiene of the United States Public Health Service and the Division of Industrial Hygiene of the Illinois Department of Public Health[1] should be of interest to all those who are concerned with this question wherever it occurs. The report contains a description of the foundry industry and of the various operations which are carried out, followed by details of environmental and medical studies made by medical-engineering teams. In the environmental study 1100 samples of air-borne dust were collected and examined. It was found that in 90% or more of the samples the particles were three microns or less in size. The amount of free silica in the air-borne dust ranged from 13% to 29% in various operations. The free silica content of settled dust averaged 30% throughout the foundries. The amount of iron in the air-borne dust ranged from 3% to 9% for all operations except casting cleaning, for which the proportion varied from 30% to 38%. Operational dust levels at various foundry activities in general were found to be much lower than those reported in earlier investigations. Concentrations of aldehydes were low, and carbon monoxide concentrations were relatively low in most cases, but high levels occurred for short periods at pouring operations during the winter months. In general the foundries studied were clean, with adequate sanitation and housekeeping, and dust suppression measures were employed. Many buildings were well constructed, and modern production techniques were usual, but less attention had been paid to the latest methods of artificial illumination and reduction of noise. The results of medical examination of 1937 male foundry workers are of interest, as these men are believed to comprise an adequate cross-section of ferrous foundry workers in the area studied, from the standpoint of socio-economic status and exposures to hazardous materials in the occupation. The most significant clinical findings related to the respiratory system. Pulmonary fibrosis of occupational origin was found in 9·2% of the men; in 7·7% of cases it was at the second degree "ground glass" stage, and in 1·5% of cases it was nodular. The fibrosis was of about equal frequency among steel and grey iron workers. Among the latter the moulders had the highest incidence of nodular fibrosis; among the former those performing cleaning and finishing operations had the highest rate. An important finding was that it generally required at least fourteen years of exposure to produce nodular silicosis in foundry workers. Blood studies indicated that pulmonary fibrosis was associated with increased erythrocyte sedimentation rates and with raised total leucocyte counts. Significantly raised blood-pressure levels were

[1] "Health of Ferrous Foundrymen in Illinois", by the Division of Industrial Hygiene, United States Public Health Service, and the Division of Industrial Hygiene, Illinois Department of Health; Public Health Service Publication Number 31; 1950. Washington: Federal Security Agency, Public Health Service. 9" x 5¾", pp. 130. Price: 75 cents.

found to be related to increasing degrees of pulmonary fibrosis. The incidence of the reinfection type of tuberculosis was similar to that of comparable groups in the general population in the same area. No eye abnormalities were found which could be ascribed to the occupation. Skin disease, probably of occupational origin, was found in 1·7% of cases. The only change in oral structures was attrition of the tooth surfaces, apparently the result of dust.

Certain important conclusions arise from the correlation of the clinical and environmental findings. The report states that there is reason to believe that dust conditions in the foundries studied had improved in the past ten to twenty years; thus it is likely that in many cases the pulmonary fibrosis observed was due in great part to higher dust concentrations which probably existed ten, fifteen or even more years previously in the foundries. However, it was considered that the conditions noted generally left room for improvement in the control of silica and other hazards, and the following recommendations were made:

Exhaust systems and dust collection equipment should be given proper maintenance. When buildings are to be remodelled or new ones built, consideration should be given to the location of various operations in order to minimize the number of workers affected by the high dust producing operations. Very dusty operations should be scheduled when few workers are present. Local exhaust ventilation should be employed when mechanical shakeout equipment is used. Exhaust ventilation should be employed with portable grinding. Adequate ventilation should be provided to prevent excessive concentrations of carbon monoxide during pouring operations and around furnace charging. Particularly noisy machines should be isolated whenever possible, or appropriate acoustical treatment should be employed where they are located. Modern lighting techniques should be employed to improve artificial illumination.

These recommendations, although intended primarily for the 18 Illinois foundries investigated, provide a useful summary of points that are likely to require special emphasis in the industry generally.

SUBACUTE BACTERIAL ENDOCARDITIS.

In February, 1945, the Penicillin Trials Committee of the Medical Research Council of the Privy Council appointed 14 centres in Great Britain to study the value of penicillin in the management of subacute bacterial endocarditis, and by January, 1949, 442 patients had been treated under the scheme. In the records of the patients treated is a great deal of detail relating not only to the effect of penicillin, but also to the influences of age, sex, various underlying heart lesions and other factors in subacute bacterial endocarditis. This has recently been analysed by J. E. Cates and R. V. Christie.[1] The main results of the treatment under the scheme have already been presented by Christie in a series of articles in the *British Medical Journal*,[2] and as most of our readers will have had access to these we need not repeat the information. Indeed, the status and details of the penicillin treatment of subacute bacterial endocarditis no longer require comment. Most of the data provided by Cates and Christie in the latest paper are of a different character. It can probably be best referred to in bald summary. The 442 patients whose records were analysed by Cates and Christie were observed from 1945 to 1948. The great majority (408) yielded positive results from blood culture before treatment began, and it is with these that the paper is mainly concerned. The ages ranged from seven to seventy-four years, but 62% of the patients were between fifteen and thirty-five years of age. The sexes were equally affected. The underlying heart lesion was acquired in 87% of cases and congenital in 13%. Disease of the mitral valve alone was twice as common in female as in male patients, affecting particularly women between fifteen and thirty-five years of age. Disease of the aortic valve alone was five times as common in male as in female patients, and disease of both valves affected the sexes equally. The sex incidence of congenital lesions was equal, but ventricular septal defect was commoner in the male, and patent *ductus arteriosus* was commoner in the female. Seven patients were found at autopsy to have bicuspid aortic valves. The ætiology of the acquired lesions was probably rheumatic in 90% of cases, whereas syphilis was the underlying cause in only one case. Hypertensive heart disease was the cause in only one case, and in no case was the underlying cause thought to be myocardial infarction. In no case was it thought that a previously normal heart was affected. The infecting organism was an α-hæmolytic streptococcus in 87% of cases, and a non-hæmolytic streptococcus in 7%. In a representative group of 215 cases a dental focus of infection or a history of dental extraction was present in 48%, and some other focus was found in another 14%. The initial symptoms were those of fever in 63% of cases, heart failure in 30%, peripheral embolism in 20%, joint pains in 17%, and pulmonary embolism in 10%.

As a result of the analysis of the series, it is recommended that the minimum dosage of penicillin should be 2,000,000 units daily for four to six weeks. A larger daily dose should be given if the resistance of the infecting organism is four or more times that of the Oxford staphylococcus. With highly resistant organisms massive doses of penicillin may fail to eliminate the infection. It was found that patients who relapsed did so within twenty days after the end of treatment in 75% of cases, and within a month in 92% of cases. In seven of the 14 cases in which a second attack occurred between eight months and five and a half years after treatment, the second organism was similar to the first. Cates and Christie state that after six months of apparent cure the risk of a delayed relapse or of reinfection is 2% *per annum*.

Complications were fairly frequent. There was a major arterial embolism in 35% of cases, and in half of these it was cerebral. Coronary embolism was recognized in 2% of cases during life, and was found in 13% of autopsies. The incidence of pulmonary embolism was 35% in cases of congenital heart disease, and 10% in cases of acquired heart disease. Auricular fibrillation was recorded at some stage in 4·5% of cases. There was an infection of the renal tract in 6% of cases.

Of the 195 patients who died, infection had not been controlled or had recurred in 23%; many of these had received inadequate treatment. Heart failure was the commonest cause of death, occurring in 63% of fatal cases. In the remaining cases death was due to arterial embolism (13%), hæmorrhage (10%), uræmia (9%), pulmonary embolism (2%), rheumatic carditis (2%), pneumonia (2%), and other causes (14%). There was more than one cause for 16% of deaths. Of the deaths, 14·5% occurred during treatment and another 27·4% in the first six months after treatment. Thereafter the death rate fell remarkably, and in subsequent years an average of only 4% of the survivors died *per annum*. Of the various factors affecting prognosis, the presence of heart failure before treatment was the most important. Other factors were age, sex, the site of the lesion and the question whether it was acquired or congenital, the state of nutrition, and the duration of infection.

Thirty-four patients with negative results from blood culture were given penicillin; in most of these there was good evidence of bacterial infection, for fever responded to penicillin in 73%, and in one-half of those who came to autopsy organisms were found in the heart valves. Only six patients of the 34 were "cured"; this low proportion was considered to be due in part to the high incidence of heart failure and in part to inadequate therapy. It is suggested that this type of patient may need a larger daily dose of penicillin than patients with positive findings from blood culture.

There is a great deal more detail in Cates and Christie's paper, which those interested should read for themselves. The patiently collected data will probably remain a standard source of reference for a long time.

[1] *The Quarterly Journal of Medicine*, April, 1951.
[2] *British Medical Journal*, March 16, 1946; January 3, 1948; October 29, 1949.

Abstracts from Medical Literature.

PÆDIATRICS.

Terramycin for Meningitis.

ARCHIBALD L. HOYNE AND EMMANUEL R. RIFF (*The Journal of Pediatrics*, August, 1951) describe the use of terramycin in the treatment of meningitis. They state that 14 consecutive patients suffering from meningococcal meningitis were treated with terramycin exclusively. The ages ranged from one to thirty-six years. There were no deaths. Seven of the patients had no lumbar punctures, but the diagnosis was proved in all 14 cases by laboratory procedures. Seven patients each had one spinal tap. Every patient received the initial dose of terramycin intravenously. With a dilution of one millilitre of 5% dextrose solution to each milligramme of terramycin, thrombosis occurred but once among 10 patients. The average number of days of treatment was 7·6, and the average total dosage of terramycin was 8·5 grammes. Although recovery often seemed to be complete within six days, the average period of hospital stay was 11·2 days. There were practically no unpleasant reactions from the drug. The authors believe that these are the first meningitis patients treated exclusively with terramycin that have been reported. In addition, three patients with influenzal meningitis were treated successfully with a combination of terramycin and sulphadiazine. One of these patients, admitted to hospital in a comatose condition and with a temperature of 105° F., made a spectacular recovery in a week's time. One patient with pneumococcal meningitis is now being treated, and he has shown an excellent response to terramycin without other medication.

Anticonvulsant Drug Therapy and Behaviour Problems.

BENJAMIN PASAMANICK (*Archives of Neurology and Psychiatry*, June, 1951) describes a series of children with behaviour problems who have abnormal electroencephalograms. He discusses the relative effects on the behaviour of these patients of various drugs—"Dilantin", mesantoin, "Tridione" and phenobarbital; the result was uniformly disappointing. Some of the patients, though not improved with these drugs, responded favourably to amphetamine; the author recommends it for trial.

Permanency of Glutamic Acid Treatment.

F. T. ZIMMERMAN AND B. B. BURGEMEISTER (*A.M.A. Archives of Neurology and Psychiatry*, March, 1951) report on a study of glutamic acid treatment and its effect on mental functioning as shown by psychometric tests, and also over different intervals of time. Originally they studied 69 children and adolescents, but only 38 were available for retesting two and a half to three years after they had ceased treatment. The average age of the patients was eleven years and eight months, and the average mental age was seven years one month (intelligence quotient 61·58). In six months of therapy the mental age rose to eight years three months, and the intelligence quotient gained 6·84 points. This growth in mental age was more than twice the rate in the normal child. (The tests were verbal intelligence tests; on the performance tests the average intelligent quotient was raised from 62·9 to 68·89.) In the second six months of therapy the verbal intelligence quotient rose only 1·25 points, making a total of 8·29 points for one year. The performance intelligence quotient in the second six months of therapy equalled or exceeded the intelligence quotient gain in the first six months. The total gain was 9·59 points in twelve months. Treatment was discontinued, and further testing was carried out after two and a half to three years. It was discovered that the patients held their large treatment gain in intelligence quotient remarkably well during the interval following cessation of therapy. It was found that the verbal intelligence quotient gain was more important in determining the permanency of improvement than was the actual length of treatment. On the performance tests, however, length of treatment was the positive factor determining permanency of effect. The authors state that the failure of other investigators to obtain positive results with glutamic acid is explained by lack of technical precision in giving the drug. They state that results similar to their own have been obtained in both human and animal fields.

Congenital Myasthenia Gravis.

R. I. MACKAY (*Archives of Disease in Childhood*, August, 1951) discusses congenital *myasthenia gravis* and reports a case. He states that this disease is rare in childhood, but cases reported can be analysed in three groups. The first group consists of infants who are born of mothers suffering from the disease and who show the transitory myasthenic state during the first few months of life, with general feebleness, poor sucking and swallowing reflexes, drooping eyelids, a mask-like facies and sometimes sudden fatal collapse. When such infants were treated for the first two weeks of life with "Prostigmin", survival and recovery were usual. If "Prostigmin" was not continued, the infants usually died, some after a sudden collapse. This condition is thought to be due to the transplacental passage of a curare-like substance, which affects the baby at birth, but which is destroyed in some manner and leaves the child unaffected in later life. In the second group, three cases of congenital *myasthenia gravis* have been reported in which the mothers were not affected, but the disease was present in the babies from birth. Treatment needed to be continued, and progress was satisfactory as long as it was continued. The third group of cases should be called "infantile" rather than "congenital", though the onset of symptoms is noted so early in life that a congenital disorder may be suspected. The author reports a case in which symptoms were noted in one of dissimilar twins. The baby was weak from birth, did not suck well and lagged very much behind her sister in sitting up and walking. At the age of three years she had bilateral ptosis and weakness of the legs. She ate slowly, tired more quickly and never hurried. She would fall clumsily and have difficulty in getting up again. She tended to have an expressionless face. Her intellectual activity was better than that of her twin. Persistence of grip was poor, and repetition movements were not well carried out. Her response to subcutaneous injection of one milligramme of "Neostigmin" methyl sulphate was dramatic and diagnostic. She remained well on a dose of 10 milligrammes of this drug given by mouth three times daily and became an active, vigorous, energetic child.

Electrocardiograms in the First Two Months of Life.

R. I. FURMAN AND W. R. HALLORAN (*The Journal of Pediatrics*, September, 1951) report a series of 70 electrocardiograms prepared from 52 normal infants in the first two months of life. Twelve leads were employed. Analysis of these records revealed the following findings. The mechanism, heart rate, *P-R* interval, *QRS* duration, duration of electrical systole, *S-T* junction and *P* and *Q* waves are essentially constant during this period. The *T* wave has unique characteristics in the first few days of life, being of low voltage and showing inversion in variable leads, but it conforms to the hitherto accepted standards of behaviour after the end of the second week, the second week being a type of transition period. The relative right ventricular predominance characteristic of the first two months undergoes considerable diminution during the third week of life, a change most easily demonstrated by the augmented unipolar extremity leads. The precordial *QRS* complexes in the first two weeks of life can normally assume so many different forms that they are of limited value in interpretation. The data are presented and discussed in such a manner as to facilitate interpretation of electrocardiograms in the first two months of life.

Cephalohæmatoma in the Newborn.

M. D. INGRAM, JUNIOR, AND W. H. HAMILTON (*Radiology*, October, 1950) report a study of cephalohæmatoma of the newborn over a five-year period. They observed 126 cases in a total of 7563 deliveries, an incidence of 1·66%. Of the 126 cases, 58 involved the right parietal bone and 36 the left parietal bone, 17 were biparietal and 15 were occipital. None were found in the frontal or temporal bones. They state that various factors have been suggested as causes of neonatal cephalohæmatoma. In this series of cases the following factors were considered: birth weight of the infant, sex of the infant, prenatal administration of vitamin *K*, fœtal presentation, maternal parity and instrumental delivery. The affected babies were heavier on the whole than those unaffected, and no cases were found in premature babies. Of the affected children, 79 were males and 47 females, a distribution of borderline statistical significance. The mothers of 51% of the infants with cephalohæmatoma had received vitamin *K*, and 49% had not, facts tending to disprove the theory that hypoprothrombinæmia in the newborn infant is a predisposing factor. The fœtal presentation seemed to be of no significance. Among the babies delivered by forceps, cephalohæmatoma was commoner in the children of primiparous than of multiparous mothers. Among the deliveries without forceps the difference between the two groups of

mothers is not significant. For the whole group forceps delivery significantly raised the incidence. The authors point out that this condition must be distinguished from encephalocele, which is almost always mid-line with an underlying hole in the skull, and from subcutaneous hæmatoma with a depressed fracture of the skull. The diagnosis of cephalohæmatoma is confirmed by the fact that its boundaries are limited by the periosteum of the bone involved.

Poliomyelitis and Physical Activity.

R. M. ALBRECHT AND F. B. LOCKE (*The Journal of the American Medical Association*, June 30, 1951) have studied 200 cases of poliomyelitis from the point of view of physical activity from three days before to a number of days after the onset of illness and the degree of residual paralysis five and a half to seven months after onset. They state that deaths and severe paralysis in children are not related to the degree of physical activity either shortly before the onset of illness or at any time during the illness. Deaths and severe paralysis in adults may be attributed in part to the degree of physical activity in the meningeal stage. Age is a major factor in the prognosis of poliomyelitis. Adults, irrespective of age, are more severely affected than children. Factors other than age and activity are of major importance in the prognosis of poliomyelitis.

Poliomyelitis and Transportation.

M. B. BRAHDY AND S. H. KATZ (*The Journal of the American Medical Association*, June 30, 1950) report the fatality rates for a group of patients with poliomyelitis who were transported to hospital over long distances and for a comparable group who were transported short distances. They conclude from the results that transportation over long distances may be harmful to a patient in the acute stage of poliomyelitis.

ORTHOPÆDIC SURGERY.

The Causative Mechanism in Morton's Metatarsalgia.

J. D. MULDER (*The Journal of Bone and Joint Surgery*, February, 1951) has drawn attention to two observations which he believes can be usually made in every case of Morton's disease. The first observation can be used as a diagnostic clinical test. The patient's foot is clasped around the metatarsal heads with the fingers of the left hand while the thumb of the right hand exerts firm pressure on the sole of the foot at the site of the suspected neuroma, usually between the third and fourth metatarsal heads. On alternation of pressure with the fingers of the left hand and of the right thumb, there can be felt a small mass which is pressed in between the two metatarsal heads by the thumb and pushed back into the sole of the foot by lateral compression of the metatarsal heads with the fingers. If this compression is done with some force, the mass may be pinched for a moment between the metatarsal heads before it is pushed out. If this mass contains or is formed by a neuroma, the characteristic pain coincides with a palpable click caused by the tumour escaping into the sole of the foot. The objective sign—the click—is found many times more frequently than the subjective sign—the sudden pain in the toes. The second observation can be made at operation. When the neuroma is laid bare by a longitudinal incision in the sole between the metatarsal heads, it can be easily pushed into the intermetatarsal space and is seen to be pinched and afterwards pressed out upon lateral compression of the metatarsal heads by the surgeon's hand. This is accompanied by the same click that has been mentioned above. If the neuroma is carefully removed by gentle dissection it will be found to be adherent to the intermetatarsal bursa and, indeed, to be so intimately connected with the plantar wall of the bursa that it cannot be removed without opening of the bursa. The author considers that the neuroma is caused mechanically by repeated pinching of the plantar nerve between the metatarsal heads during the abnormal movements associated with weak transverse arches.

Muscle Relaxants in the Diagnosis and Therapy of Acute Back Disorders.

E. B. SCHLESINGER AND F. E. STINCHFIELD (*The Journal of Bone and Joint Surgery*, April, 1951) believe that at times the vicious cycle of pain and muscle spasm may so exaggerate the symptom complex of the acute low back syndrome that it is difficult to consider the muscle spasm as purposeful. They have found that "Myanesin" given intravenously in a 2% solution is capable of rapidly dissolving muscle spasm in the "acute disk syndrome". A series of patients with acute low back and radicular pain were studied before and after the injection of this drug. It was found that pain and limitation of movement of the limb could be altered with gratifying symptomatic relief. In certain instances this response persisted and, when followed by conservative treatment, led to long-term cure. In others there was abrupt return of pain and limitation of movement as soon as the drug concentration dropped below therapeutic levels. In such cases the patients invariably failed to respond to conservative treatment and eventually came to operation. The authors believe that the correlation of test response to the drug and prognosis was sufficiently striking in a series of 64 cases to warrant discussion as a possible clinical test. In the group characterized by no response or a rapid return of signs and symptoms immediately after injection, patients generally failed to respond to any period of conservative management. Their operative records reveal evidence of root compression of such degree as to make conservative attempts at decompression unfeasible.

An Improved Type of Arthroplasty of the Hip Joint.

ANTHONY F. DEPALMA (*The Journal of Bone and Joint Surgery*, April, 1951) states that arthroplasty of the hip joint was designed primarily for cases of absorption of the neck of the femur following non-union. However, the results have proved so gratifying that the method is now employed for other pathological lesions of the hip joint, for which hitherto a vitallium cup arthroplasty, such as that described by Smith-Petersen, has been considered necessary. Essentially, the operation consists of removal of the head and neck of the femur, severing of all muscle attachments from the greater trochanter, osteotomizing of the shaft of the femur four inches from the top of the greater trochanter, tilting of the upper fragment medially to restore the normal angle of the neck of the femur, and fixing of the fragments in this position by a Newfeld nail. The greater trochanter is then covered with a vitallium cup and placed in the acetabulum. Finally, with the extremity slightly abducted, the *gluteus medius* and *gluteus minimus* are reattached through drill holes to the lateral aspect of the distal end of the proximal fragments. The author considers that this procedure, by providing a normal angle between the new neck and shaft of the femur, produces a joint approaching closely the architecture of the unaffected hip joint; furthermore, since the abductor muscles are transplanted downwards, the efficiency of this group of muscles is not impaired seriously. This operation has been performed in 17 cases since January, 1947; 14 cases are analysed in which the post-operative period has been one year or more. No deaths were caused by the operation. The author considers, however, that this type of arthroplasty is an extensive surgical procedure; it should be employed only for patients with relatively good general physical fitness who are willing to cooperate fully after the operation. In the author's series results have been poor in four cases, excellent in five, good in two and fair in two. Shortening of the extremity has not exceeded three-quarters of an inch. All patients have exhibited a slight limp, but this has not precluded development of a good free gait approaching the normal.

Recurrent Subluxation of the Ankle.

MACK L. CLAYTON *et alii* (*The Journal of Bone and Joint Surgery*, April, 1951) believe that recurrent subluxation of the ankle caused by torn lateral ligaments is more common than is realized. They state that it is necessary to determine whether or not the lateral ligaments are completely torn in a case of acute sprained ankle. In most cases the diagnosis must be based on X-ray examination of the ankle with the foot in forced inversion. It is important that the peroneal muscles be relaxed when X-ray pictures are taken. The authors have found that injection of five to ten millilitres of 2% procaine solution around the peroneal nerve in the region of the head of the fibula causes peroneal paralysis in from five to ten minutes. Painless unresisted inversion of the ankle is then possible with all factors of resistance excluded except those of the lateral ligaments. The authors believe that this is a safer and more reliable procedure than the injection of procaine locally around the ligaments. Peroneal nerve block has also been used to test for tibio-fibular diastasis in severe ankle injuries. The authors have performed *peroneus brevis* tenodesis in seven chronic cases of recurrent subluxation of the ankle. In five cases the patients have been followed for over one year. All have been relieved of twisting of their ankle. In all cases the ankle was stable and a full range of movement was regained.

Research.

THE ANTI-CANCER COUNCIL OF VICTORIA.

A COMBINED MEETING of the Medical and Scientific Committee and the Executive Committee of the Anti-Cancer Council of Victoria was held on August 6, 1951, at the Royal Australasian College of Surgeons.

Report on Current Cancer Research in England and the United States as Observed during a Visit, January to July, 1951.

DR. R. MOTTERAM expressed his gratitude to the Victorian Anti-Cancer Council for giving him a period overseas. He said that it had been of great personal benefit to him, and he hoped that in the future he would be able to further the experimental study of cancer in Victoria. Dr. Motteram said that he had made the study of the experimental procedures used in certain aspects of cancer research the chief purpose of his trip. He believed that the standard of morbid anatomy and morbid histology in Melbourne was such that time spent in that department overseas would be of little advantage to him. Brief visits to the departments of morbid anatomy in well-known centres served to confirm that opinion. His time in London had been mainly spent in the laboratory of the Imperial Cancer Research Fund at Mill Hill. Some account of the general set-up of that place might be of interest, should anything of the sort be contemplated in Victoria. The building housed an excellent library of a specialized nature. Separate rooms were provided for a biochemist, a physiologist and a histopathologist. More extensive quarters were occupied by a group working under the director, Dr. James Craigie, on problems of the growth of mouse tumours. The animal rooms were an important feature of the place. Dr. Craigie was interested in developing quantitative methods for the study of problems of mouse tumour transmission. Methods such as grafting and the injection of tumour minces did not lend themselves to accuracy in assessing tumour growth. Dr. Craigie therefore used an anaplastic mouse tumour 37S "Sarcoma", which had been adapted to grow in the ascitic fluid excited by its primary growth on peritoneum. Those tumour cells occurred singly in the ascitic fluid, and in favourable mice there was very little admixture of macrophages. The number of viable tumour cells transplanted could be estimated accurately by counting under the phase contrast microscope, and from the known period of time taken for the mitotic cycle the time taken to get a visible subcutaneous tumour could be predicted. Problems such as the survival of tumour cells after they had been subjected to a variety of physical agents could be studied in that manner. One was then more likely to be able to draw valid inferences from the observed results than was the case when grafts and minces were used. Dr. Motteram said that he had cut sections of the area of the subcutaneously injected ascites tumour cells from periods of hours to days after implantation. He had been able to observe the early mode of growth of those cells and the effect of various suspending fluids on the process.

Dr. Motteram went on to say that he had spent the latter part of his stay in London at the Chester Beatty Institute. There one of the chief activities was the synthesis of "radiomimetic" drugs of the general type of the nitrogen mustards. Such drugs had a twofold interest. One was to produce a chemotherapeutic agent for treating cancer. The other was to study the fundamental biochemical and biological changes induced in cells by those substances. It was found that the "radiomimetics", just like most growth inhibitors, were carcinogenetic, and experiments with drosophila showed that they were also mutagenic. It was hoped that a close study of those substances would produce an avenue of approach to the understanding of the fundamental changes involved in carcinogenesis. New chemotherapeutic substances were tested against the Walker rat carcinoma, and if the results were favourable, the substances were given clinical trial at the adjoining Royal Cancer Free Hospital. R48—a nitrogen mustard capable of being given orally—had been developed, but clinical trials showed it to be inferior to the commonly used substance. It was a little disappointing to note that there had for some years been no advance beyond the nitrogen mustard group of substances. Triazide (synonym triethylenemelamine), a finisher used in the rayon industry and possessing reactive groups the same as a solution of nitrogen mustard, was being used in England and America. It possessed certain advantages, in that it need not be given by a running intravenous drip method. Also, if precautions were taken against its destruction by stomach acid, it could be given orally. A laboratory check of white cell counts was essential. Dimithoxy sulphone, synthesized by Geoffrey Timmins at the Chester Beatty Institute and labelled "GT41", had been found useful as a depressant of myeloid tissue in chronic myeloid leuchæmia.

Dr. Motteram then said that in New York he had been attached to the Sloan Kettering Institute. There in the last few years some 3000 substances had been screened for activity in suppressing tumour growth and leuchæmia in mice and rats. Trial was first made against the mouse sarcoma 180, and anything showing a suggestive effect was then tried against a spectrum of eight different tumours. The variation in sensitivity of different tumours within the same species, and of the same type of tumour in different species, was quite remarkable. That was noted especially in the class of chemotherapeutic agents, which acted by virtue of competing with an essential metabolite to which it had a similar structure. The best known of those substances were folic acid antagonists—the amino pterins. A guanine antagonist, 8 azaguanine, and an adenine antagonist, 2:6 diamino purine, had had some success in rodent tumours, but when tried clinically had been found to be very toxic and had produced little effect on any type of human cancer. The antimetabolites had been of purine type, mainly because of suggestions that the purine metabolism of cancerous tissue was of abnormal type. Probably it was more a question of excessive production of nucleic acid precipitating cell division than any alteration in type of nucleic acid. Indeed, much fine work had shown that both substrates and enzyme systems involved in the metabolism of cancer tissue were essentially similar to normal tissue. Therefore, when interfering with the metabolism of the rapidly dividing cancer cell by any administered substance, one would also damage those normal body cells which underwent frequent division, notably the hæmatopoietic marrow, the generative epithelium of gonads and the epithelium of duodenum and ileum. Therefore it was unlikely that that approach could produce anything other than palliative results. Agents changing the environment of hormonal dependent cells, such as œstrogens and androgens in breast cancer and œstrogens in prostatic cancer, continued to be useful as palliatives.

Dr. Motteram further said that a novel line of inquiry carried on at the Sloan Kettering Institute was the production of an oncolytic virus—in other words, such adaptation of a virus that it multiplied exclusively in tumour tissue, with the resultant destruction of the tumour. Much hope was held out for that technique, and he had had himself attached to Dr. Alice Moore, who was directing the work. It had been found that the oncolytic effect was associated with neurotropism, and the most successful virus used so far was that of Russian encephalitis. Dr. Moore had found that continuous passage in mouse sarcoma 180 of that virus caused its oncolytic ability to increase, but even though the tumour was destroyed in four days, the neurotropism was not diminished and the mouse died in seven days from encephalitis. Continuous passage of the virus in the Wagner osteogenic sarcoma of mice altered the virus from initially having no effect on the tumour to a condition whereby it now destroyed it. Efforts were being made to produce a pure oncotropic virus, on the assumption that a mutant strain was present. There remained then the task of adapting the virus to human tumour. For that the tumour had to be grown by heterologous transfer. At the Sloan Kettering Institute that was done by irradiating rats with X rays with a dosage sufficient to produce a leucocyte count of approximately 2000 per cubic millimetre. That was taken as an indication that the animal was incapable of reacting to heterologous tissue for at least a week; after that one further period of irradiation could be given. Then the tumour had to be transplanted. Professor Greene at Yale grew human tumours in the anterior eye chamber and the brain of guinea-pigs. Greene believed that malignant tumours lacked species specificity and that growth could be taken as evidence of malignancy.

With regard to the assistance which could be given to the surgeon and radiotherapist by the histopathologist, Dr. Motteram said that the place of chief interest was the Bland Sutton Institute. There Professor Scarfe for many years had been attempting to correlate the histological pattern of breast tumour with prognosis. He used the usual classical concepts based on Grenough's work. He found that the histological pattern was of more importance in predicting survival time than was the stage of the disease or the duration of the history. Glucksmann, at Cambridge, had obtained similar results for carcinoma of the cervix, and in addition took a further biopsy after seven days in those cases in which irradiation was being used. "Dif-

ferentiation" (keratinization), cell degeneration and a fall in the number of cells undergoing mitosis were taken as an indication that the tumour was likely to respond to irradiation. Koller at the Chester Beatty Institute held that the direct effect on the malignant cell was not the whole story, but that the reaction induced in the stroma was of equal importance in inducing tumour regression.

Dr. Motteram said that the only experimental work actually being done on human subjects that he had seen was at the Laguna Honda Home in San Francisco. There the National Cancer Institute supported an experimental oncology unit. Human volunteers suffering from incurable cancer were the experimental subjects. Dr. Bierman, in charge of the unit, had shown by exchange transfusions between chronic leuchæmics and cancer patients that the normal lung caused a rapid disappearance of excess circulating leucocytes. He therefore postulated a failure of removal of leucocytes in leuchæmia. Dr. Bierman also cannulated the thoracic duct in chronic lymphatic leuchæmia, and, contrary to expectations, found a normal content of lymphocytes in the issuing lymph.

Dr. Motteram, in conclusion, said that he wished again to thank the Council, and that he was looking forward to starting some experimental work along the lines elaborated in his report.

DR. JOHN O'SULLIVAN, from the chair, thanked Dr. Motteram for attending, and suggested that a report should be circulated, not only to members of the Anti-Cancer Council and its committees, but also to a wide circle of the medical profession. Dr. O'Sullivan asked Professor MacCallum to support his vote of thanks.

PROFESSOR PETER MACCALLUM stressed the need for greater effort in Australia in the field of research, and said that an institute for cancer research should be established as the country's contribution to the attack on the cancer problem. He believed that a close search would reveal that the right men were available in Australia to carry out such work.

MR. BALCOMBE QUICK asked Dr. Motteram whether the greater emphasis abroad was placed on the problem of causation of cancer, or, as Mr. Quick had gathered from Dr. Motteram's address, on research in empirical therapeutic substances.

Dr. Motteram, in reply, explained that the institutes abroad were supported by public funds, and held that they must justify their existence in the public's eyes by providing some palliative or cure of cancer. However, Dr. Motteram pointed out that biological work was being carried out extensively, and that he felt that the two points were actually interwoven.

Report on the Use of Radioactive Phosphorus at the Royal Melbourne Hospital.

DR. R. KAYE SCOTT presened a report which he had prepared for the Director of the Commonwealth X-Ray and Radium Laboratory on the use of radioactive phosphorus at the Royal Melbourne Hospital. He said that radioactive phosphorus had but limited therapeutic use. The prime indication for treatment was *polycythæmia vera*, and satisfactory remissions had followed treatment of the limited number of patients presenting with that disease. Shortage of supplies initially dictated a policy of intravenous injection of P^{32}; oral administration was possible, but absorption was not complete. The dosage required was variable, and the experience of overseas workers had dictated a policy of safety by which reasonable small doses were given, which could be repeated on subsequent occasions if the initial response was not adequate. Arrangements had been made by the Commonwealth X-Ray and Radium Laboratory for a supply of radioactive phosphorus to be sent to country doctors who had referred their patients to an accredited consultant who, after examination of the patient, was able to prescribe dosage. The consultant was responsible for gathering follow-up reports and records of the patients, and for prescribing further dosage as necessary, which was sent to the country for administration. Several patients had been examined at the Royal Melbourne Hospital clinic under the terms of that scheme.

Dr. Kaye Scott went on to say that a number of patients suffering from leuchæmia had been treated with radioactive phosphorus. They had been patients generally in the late stages of their disease, with marrow failure, and the treatment had not been of significant benefit. Owing to limitations of supply, patients in the earlier stages had not been submitted for treatment, as routine methods of irradiation had been easily applied. Recent reports had shown that patients with chronic lymphatic leuchæmia might be slightly better treated with P^{32} than with X-ray therapy; the opposite held for chronic myeloid leuchæmia.

A small number of patients with medullary reticuloses had been treated. It had been observed that patients with reticulosarcoma had shown practically no response. Examination in collaboration with Dr. R. Motteram, of the Austin Hospital, of sections from some of those patients had shown that the nuclei of the malignant cells were almost devoid of desoxyribonucleic acid and in general contained little obviously staining chromatin material. The absence of the evidence of active phosphorus metabolism by the malignant cells had been in striking accord with the lack of clinical response. On the other hand, some dramatic recessions of masses of lymphosarcomatous type had been noted, and a small number of patients with that disease had received great palliative relief, with shrinkage of neoplastic masses and return of well-being over periods of many months. Treatment had been administered on a routine basis to such patients at intervals of three months. Examination of biopsy material from those patients had shown that the nuclei were in general of deeply staining type, and that the cells appeared to contain large amounts of desoxyribonucleic acid, a feature conforming with the clinical evidence of the radiosensitivity exhibited.

Dr. Kaye Scott further said that stringent precautions had been taken in the radiotherapy department, with both radioactive phosphorous and radioactive iodine, to develop handling and administration techniques which avoided all possible radioactive contamination of personnel or of permanent fittings of the department. The help of the physicists from the Commonwealth X-Ray and Radium Laboratory in developing and policing the administration technique had been greatly appreciated.

Dr. Kaye Scott said that the number of doses of P^{32} given at the Royal Melbourne Hospital were: 1948, 39 (eight patients); 1949, 24 (eight patients); 1950, 28 (nine patients); 1951, 14 (four patients); the total to date was 105.

He presented the following table (Table I) setting out the details concerning the patients treated. Of the total number of 25 patients treated, 12 had died and 13 were still continuing.

TABLE I.

Disease.	Number of Patients Treated.	Result.
Polycythæmia	9	1 died. 1 failed to report. 7 well.
Lymphatic and myeloid leuchæmia.	7	5 died (2 with myeloid leuchæmia). 2 well.
Lymphosarcoma	4	2 died. 2 well (recently affected).
Reticulosarcoma and medullary reticulosis.	5	4 died. 1 well (medullary reticulosis).

Report of Work with Radioactive Iodine at the Royal Melbourne Hospital.

Dr. R. Kaye Scott next presented a report of work with radioactive iodine at the Royal Melbourne Hospital which he had presented for the Director of the Commonwealth X-Ray and Radium Laboratory. Dr. Kaye Scott said that work with I^{131} had commenced in the radiotherapy clinic some three years earlier. Active collaboration by the Commonwealth X-Ray and Radium Laboratory made tracer testing possible, and the necessary electronic apparatus had been made available to the hospital by the laboratory. An operating technician of the radiotherapy department had carried out the counting operations under the direction of the laboratory physicists, and patients for investigation or treatment had been referred from the various departments of the Royal Melbourne Hospital, and some patients had come from other hospitals. Initially the work was restricted to tracer tests to determine toxicity, and Oddie had early developed a series of mathematical expressions covering known features of iodine uptake, metabolism and excretion. Much work had been carried out in comparing the results of various tests on subthyreoid, normal and "toxic" patients, with results of clinical and biochemical tests of the same patients' state of toxicity, and a comparison with the testing criteria developed by other workers had been made. With development of the work, it was thought that a team was

needed representative of the clinical, physical and research interests involved. Late in 1950 a Thyreoid Panel was therefore formed at the Royal Melbourne Hospital consisting of the following: Dr. R. Kaye Scott, the radiotherapist, Dr. J. P. Madigan, his assistant, Dr. W. E. King, physician, Dr. Hurley, his assistant, two physicists, Mr. Clark and Mr. Aujard (Dr. Oddie having retired), a pathologist, Dr. R. Motteram, *vice* Dr. Forbes, and a biochemist, Mrs. Winikoff. The cooperation of Dr. C. E. Eddy, Professor V. M. Trikojus, Professor Peter MacCallum, Professor E. S. J. King, Miss Splatt and the Royal Melbourne Hospital staff was gratefully acknowledged.

Dr. Kaye Scott went on to say that the necessary supplies of I^{131} had been made available by the Department of Health through the Commonwealth X-Ray and Radium Laboratory. The panel had met each Friday for a discussion of case material, and the results of the physical, biochemical and clinical investigations had been correlated. The work had resolved itself into four categories: (*a*) tracer tests for toxicity, (*b*) tracer tests for thyreoid tissue in abnormal sites, (*c*) therapeutic doses for non-malignant conditions, (*d*) therapeutic doses for malignant conditions.

Tracer Tests for Toxicity.

Tracer tests for toxicity had been limited to the carrying out of six tests in each four-weekly period, owing to the availability of iodine and physical help. Patients from outside hospitals, other than the Royal Melbourne Hospital, had been given preference, as it was recognized that the Royal Melbourne Hospital had been favoured with the services of the Commonwealth X-Ray and Radium Laboratory in establishing a physical investigational service which obviously could not be duplicated in each metropolitan hospital. Cases of the greatest scientific interest had therefore had priority over other clinical material. All cases had been reviewed by the Panel before treatment or investigation was undertaken, and free discussions had taken place. In general, an independent estimate had been made of the clinical state of the patient by the physician, and that had been correlated with the tracer, physical, biochemical and basal metabolic tests which had been carried out independently.

Dr. Kaye Scott went on to say that the object and nature of the tracer work had been an attempt to verify by clinical experiment the mathematical studies of thyreoid function as propounded by Dr. Oddie. Efforts to determine the significance of the various parameters obtained had been made, and the results had been correlated with other work along similar lines. A technique for obtaining accurate assessment of toxicity by the use of radioactive iodine had been developed, and it was hoped to carry those clinico-physical tests to such a level of accuracy that it would be possible to replace the relatively inaccurate basal metabolic rate test. It was realized that some of the investigations used were more complex than other contemporary studies, but it was held that there was no reason for curtailing the testing of the mathematical theories propounded as a straight piece of research. Obviously, a considerable number of patients had to be tested if reliable figures were to be obtained. The complete tracer test of a patient along those lines took approximately a week, and it had been necessary also to develop a technique for carrying out an estimation of toxicity more rapidly, so that the time of the patient under test and of the operating and physical personnel might be saved. According to the needs of the patient, either full testing or short testing was undertaken.

Tracer Tests for Thyreoid Tissue in Abnormal Sites.

Patients presenting thyreoid tissue in abnormal sites were relatively few, and the importance of such patients was not great, but the tests carried out had fallen into two categories: (i) cases in which malignant metastases had been investigated to determine whether pick-up was present, and whether subsequent treatment with radioactive iodine was a possibility; (ii) cases in which the nature of the tumour was not definitely known, and cases of that nature, generally mediastinal tumours, had been investigated. The correct predictions which had followed tracer tests in that series had been very highly appreciated by the referring authorities.

Therapeutic Doses for Non-Malignant Conditions.

The Panel adopted the rule that patients able to be treated by standard methods should not be treated at present by radioactive iodine. That was necessary in view of the known limitations of iodine supply. At a recent Panel discussion on the subject it was held that the Panel would be justified in treating patients suffering from ordinary hyperthyreoidism with radioactive iodine if it was necessary to study the response of such patients for the determination of problems arising during the progress of the clinical researches in hand. The Panel was receiving for investigation and treatment a number of patients whose treatment by standard methods had failed. Such patients had all been accepted for treatment, and it was expected that more of those patients would be presenting in the future. However, the literature reported successful treatment of many patients suffering from hyperthyreoidism by radioactive iodine as a primary treatment method. It had to be expected that a demand for that form of therapy for local cases would therefore arise in the immediate future. But up to the present iodine supplies had only just been sufficient to allow treatment of the group of patients for whom ordinary methods of treatment had failed. The Panel believed that the present limitation on the acceptance of patients for treatment should not be continued indefinitely, and that sufficient amounts of radio-iodine should be available to allow of treatment in a wider group of cases as necessity arose.

Treatment of Malignant Conditions.

Patients suffering from carcinoma of the thyreoid with distant metastases, who were in reasonably good general condition, had been submitted to tracer tests to see whether radio-iodine therapy was practicable. Only two patients had received extensive treatment. One of those patients was referred from South Australia; the other had metastases in the spine, which made it impossible for the patient to be moved for routine X-ray therapy. The occurrence of toxic manifestations after administration of large doses at relatively long intervals demanded a routine of administration of therapeutic doses at approximately monthly intervals, on information at present available. The acceptance of any patient with carcinoma of the thyreoid for treatment with radio-iodine demanded doses of the order of 20, even up to 100, millicuries per month. That at present was outside the limits of ordinary supplies; but such patients were certainly presenting, and the problem of supply had to be considered. Carcinomatous thyreoid tissue in the presence of normally functioning thyreoid tissue might not pick up radioactive iodine. However, if a complete extirpation of normal thyreoid tissue was undertaken, or if that tissue was destroyed by therapeutic amounts of radio-iodine, then in many instances the carcinomatous tissue would subsequently pick up significant amounts of radio-iodine. If all patients suffering from carcinoma of the thyreoid with metastases therefore had either surgical or radiational ablation of functioning thyreoid tissue, then it was likely that the demand for radio-iodine for treatment of a proportion of such patients would be greatly increased.

Report from the Austin Hospital on the Use of Nitrogen Mustard.

A report was presented on the use of nitrogen mustard at the Austin Hospital. It was stated that supplies of nitrogen mustard had first come to Australia in 1948. The supplies had been received from Dr. D. A. Karnofsky, of the Memorial Hospital, and part of the initial parcel had been sent to Melbourne and part had been sent by Dr. Thiersch to Adelaide. Mustard at that time had found its greatest use in Hodgkin's disease. Less favourable reports of its use in other reticuloses had been recorded. It had been tried in most of the epithelial malignant conditions without significant success, but was in use at Brompton for the palliative treatment of inoperable carcinoma of the lung in 1947.

It was stated that nitrogen mustard was a contact vesicant, and on direct injection was apt to cause phlebitis, venous thrombosis, or delayed healing or sloughing along the puncture track. Those undesirable sequelæ had been eliminated by injecting the mustard into a set-up intravenous saline transfusion apparatus. The administration usually caused great post-injection nausea and vomiting, which generally passed off after twelve hours. Treatment was often pushed to limits producing severe marrow damage, and therefore repeated blood examinations were needed for control, with occasional examinations of the marrow.

The first Melbourne supplies were used in the cancer ward of the Austin Hospital, and considerable trouble was taken to see that the risks of contamination to operator and patient were eliminated. The working set-up there proved as satisfactory as was expected, and so all patients needing nitrogen mustard were concentrated in that hospital, in spite of serious deficiencies of bed accommodation. The work was carried out under the direction of the honorary radiotherapist, Dr. R. Kaye Scott, and the then senior

medical officer in the cancer wards, Dr. J. P. Madigan, undertook the care of the records.

The parallelism between the mode of action of irradiation and nitrogen mustard was early pointed out. The main action of the mustard was stated to be a chemical combination with various protein groups while certain enzyme systems were inactivated. Protein synthesis was early prevented, multiplying cells were particularly susceptible, and mitotic activity was inhibited to a greater or lesser degree, even up to causing late or immediate death of cells. After injection mustard passed two or three times around the circulatory system, while it was not completely absorbed for at least two minutes, and was certainly not primarily absorbed in the lungs.

At the Austin Hospital a few patients with Hodgkin's disease and with other reticuloses or neoplasms had been treated; but the main work had been in the palliative treatment of carcinoma of the lung. Abroad, the usual practice was the administration of a standard series of four injections given within a short time; but it had notably failed to cure any patients with carcinoma of the lung. Some palliative results of value had been obtained.

It was pointed out that that method of administration seemed to those working at the Austin Hospital to be wrong in principle if only palliative results were sought. If the mechanism of action was a mustard nucleoprotein combination, then it might be expected that cells in mitosis, being rich in nucleoprotein content, would be more sensitive and resting cells less so. Exactly similar considerations applied to radiation techniques, in which under similar conditions it was found most useful to apply effective doses at regular intervals. It was thought that similar principles should apply to mustard administration. Blood studies indicated that three weeks must elapse after mustard damage to hæmatopoietic tissues before recovery was reasonably complete. It was decided that injections would be given at intervals of four weeks, empirically chosen on the basis of the above-mentioned considerations. Initially, the large course of four injections was adhered to, though it was thought to be illogical. The course of three or four doses of 0·1 milligramme of nitrogen mustard per kilogram was administered each second day, and thereafter was followed by a further single injection of the same amount each fourth week. However, in all recent cases the first four injections had been given at weekly intervals during the first month, and subsequently doses were administered at monthly intervals.

It was assumed that not all cells of the neoplasm were killed by the first series of injections, and that resting cells later came into mitosis. It was the aim to attack the cells when they were in that more sensitive state, referred to by the radiobiologist as the state of mitotic sensitivity.

Patients who had shown satisfactory symptomatic control, and in whom progress of the disease had been arrested, were treated with X-ray therapy as a routine procedure at the sixth month, provided that the disease was reasonably localized. The mediastinum and the adjacent pulmonary infiltrations were included in the treatment field, while cervical glands were found to show much more reduction with X-ray therapy than with mustard injections. A further course of X-ray therapy was considered when applicable at the twelve-month stage, or earlier if special indications existed. The administration of doses of the order quoted had been adhered to, but numerous problems in regard to the most satisfactory quantity of nitrogen mustard to be used and the interval between injections remained to be solved.

Numerous manifestations of mustard toxicity in patients with carcinoma of the lung had been encountered. They could be classified in the following manner.

1. Local complications might occur—namely, complications of the venous injection; the complications of mustard sickness, nausea, vomiting and rigors. Treatment along similar lines to that used in combating irradiation sickness had been used. The various sedatives and the members of the vitamin *B* series of vitamins had been used, and pyridoxine has been found of some effect. Anti-histamine substances, such as "Dramamine" or "Benadryl", had been found of partial effect, while in accordance with the work of Ellenger, cortisone also had been used, with some, though incomplete, benefit.

2. Constitutional changes followed the administration of mustard, and these particularly involved the hæmatopoietic system. There was a rapid fall in the number of platelets, which might produce effects of purpura or hæmorrhages; a rapid fall in the number of white blood cells causing lymphopenia or leucopenia and agranulocytosis might be followed by infective complications. It had been a routine procedure to administer penicillin when leucocyte counts fell below certain empiric levels. The fall in red blood cells was seen as a delayed effect.

3. Late effects of the mustard injections had been particularly few. No effects of permanent damage to marrow had been seen as the result of the long-continued injections of mustard, in some cases lasting up to and over two years. In one or two cases the development of a psychosis had been suspected, and in another few cases evidence of peripheral neuritis had been encountered.

Only patients with conditions regarded as inoperable had been accepted for mustard therapy. In each case proof of diagnosis had been required by bronchoscopy and biopsy in addition to radiological and clinical findings. At the Austin Hospital experience had led to the conclusions that significant benefits would accrue only to those patients in the inoperable group who were in reasonably good general condition. Minor degrees of anæmia did not contraindicate treatment if that condition could be corrected by blood transfusion.

It was stated that the following rules governed contraindication and had been formulated as the result of experience at the Austin Hospital: (i) The presence of well-developed malignant cachexia and the onset of terminal stages of the disease were contraindications. (ii) The known presence of hepatic or palpable upper abdominal secondary deposits contraindicated treatment. (iii) The presence of known cerebral secondary deposits was likely to be followed by acute focal reactions, with coma and death. (iv) Massive pleural effusions indicated pleural spread, and patients with that complication had not responded. Further, a pleural effusion had appeared as a complication in some patients showing previous improvement under mustard therapy, and prompt retrogression and death had often followed. (However, Karnofsky had reported benefit from intrapleural injection of mustard in such cases.) (v) The presence of diffuse glandular involvement in cervical, axillary or abdominal regions contraindicated acceptance of the patient for mustard treatment. The presence of mediastinal glands, even if dilating the carina, or of a small bunch of supraclavicular glands, did not contraindicate mustard subject to the general well-being of the patient. Such patients might show improvement with combined radiotherapeutic procedures.

The nature of the palliative benefits shown by the patients included an immediate diminution of pain, cough, amount of sputum and hæmoptysis. Often a diminution of respiratory embarrassment resulting from recession of obstruction to airways followed mustard administration. An increase of well-being, sleep and appetite were manifestations of useful palliation. Radiological evidence of shrinkage of pulmonary opacities due to collapse or infiltration was seen, but less commonly was any real shrinkage of pleural effusion likely to occur.

Some patients had become ambulant, and had been discharged from hospital to continue routine treatment as outpatients, and treatment had been alternated with X-ray therapy, particularly if mediastinal gland masses were present. The first patient treated by that routine method had recently died after a period of nearly two and a half years' palliation. During most of that time she was able to carry on her occupation as a trained nurse, subject to intermissions for monthly injections of mustard.

Mustard was not usually able to cause any significant diminution in pressure effects due to enlarged mediastinal glands, and if such glands were present initially or as a residual feature, X-ray therapy was indicated as a complementary measure of treatment.

The results of the treatment were stated to be as follows. In all 32 patients suffering from carcinoma of the lung had been treated in the past two and a half years. They were divisible into fairly definite groups. In the first group there were ten patients. Six of these were classified as having advanced disease with multiple secondary deposits or pleural effusion. Cerebral secondary deposits had been present in some cases. None of these patients was relieved or received benefit, and all died in less than one month. The other four were in a slightly less advanced stage, and received some temporary benefit lasting but one or two months, and all died within three months. The second group consisted of patients currently under treatment for a period of less than three months. There were three patients, all showing initial relief. The third category contained eight patients, all of whom received significant relief lasting from three to six months. Of the eight, one was still alive and continuing treatment; two had not been traced after the six months' stage; five had died of their disease. In the fourth

group, seven patients had survived for between six and twelve months, and two were still living. Two had been reasonably well for six months, and had then died, one of pleural effusion and one of abdominal secondary deposits; one had died at seven months out of hospital; another had defaulted after being well for five months and had died at seven months; yet another had been well for ten months and had died at twelve months; two were still well and continuing treatment at eleven months. The fifth group consisted of four patients who had survived for more than one year, two of whom were still living. One had been well for twelve months and had died of pleural effusion at thirteen months; one had survived for two years and three months and had died of bronchial obstruction and pleural effusion (this patient was the trained nurse who had carried out her professional duties for the greater part of the two-year period); a third had survived for twelve months, but suffered from infective complications; the fourth was alive and well after twenty months, and was ambulant and showing great clinical and radiological improvement.

Two patients had received mustard treatment for carcinoma of the lung after full investigation, including a positive report on a biopsy specimen in one case. One proved ultimately to be suffering from Boeck's sarcoid, the other from tuberculosis of the lung.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE HEALTH OFFICER AND VACCINATOR.[1]

[*Australian Medical Journal* (Editorial), April 1, 1847.]

The importance, usefulness and necessity of £300 a year being taken from the pockets of the people of this colony, to a person whom they dignify with the name of Health Officer, may be estimated by the public from the following facts, which have been stated to us on authority on which we can rely: A ship from London enters the harbour in the evening—the Health Officer is engaged or not to be found—none of the passengers are allowed to land—but a boat load of people from Sydney are permitted to board the vessel, remain some time, and return to shore unobstructed!

It is also a notorious fact that sick men are frequently landed by boats from vessels which do not come up the harbour, and of which the Health Officer knows nothing!! Yet the people pay this official £300 a year to preserve them from contagious diseases that may possibly be brought by ships coming to the port! If it is necessary to our national importance to have an officer to bear such a title, and wear a blue coat with the official brass buttons blazing on it, surely the object might be effected at somewhat less expense. We would undertake to find plenty of men in Sydney who would take the title and the livery, for the sake of the latter only without any other remuneration. We beg to suggest this to those legislators who voted against the allowance of a sufficient sum to protect the colonist from the horrors of smallpox. The saving effected by the plan we propose would do all that is desirable for this purpose, and the sooner it is done the better: for if no greater vigilance is exercised by the Health Officer than such as we have described, we know not how soon we may have direful proof of the necessity of the one and the utter inefficiency of the other. It may be seeing that the individual alluded to above has lately been appointed Vaccinator with an additional salary of £100 a year, that he was, at the time when he was wanted to board the vessel, busy vaccine-lymph hunting: but he should have remembered that while he was looking for the key to lock the door, the enemy may steal in.

We beg the attention of the candle-end and cheese-paring economists in the Council to the fact, that £400 is voted by them to protect the colonists from "the pestilence that walketh at noonday", and to remind them that if such a sum is required, and is likely to be efficient for the purpose that they ought, at least, to see that we have value for our money.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

RECURRENT PTERYGIUM.

SIR: As one who has played a part in presenting a new attitude towards the problem of the pathology and surgical treatment of pterygium, I would like to congratulate Dr. J. B. Gilchrist Gibson on his sound and thoughtful article on recurrent pterygium (THE MEDICAL JOURNAL OF AUSTRALIA, November 17, 1951). For his information about the treatment of recurrent pterygium with contact X rays, I have nothing but admiration, and I hope that his technique will be noted abroad in those other countries where pterygium is of frequent and dangerous occurrence.

I must, however, join issue with him about the surgical technique and also with our Editor about a remark in "Current Comment" of the same issue of November 17, though I am duly appreciative of his recognition in this matter.

It is stated in "Current Comment" that "Gibson's experience does not seem to have been so happy. Adoption of D'Ombrain's principles has not meant an end of recurrence". My principles have not been adopted in their entirety by Gibson. Firstly, on page 664 he states, "the alternative is deliberately to shave off a thickness of the cornea beneath the pterygium". In my technique there is no alternative; it is essential to remove the diseased and degenerative layer of corneal tissue beneath the obvious overlying conjunctival tissue.

Secondly, although he very graciously states that he follows my idea of dissecting away the underlying subconjunctival tissue (which in my view is the active, reproductive element in a pterygium), he then proceeds to transplant the head of the pterygium downwards. In my opinion (and also in the opinion of my distinguished colleague, Sabri Kamel, of Egypt) this is unnecessary; further, in my own opinion it is deleterious, for the following reason: it drags down a fresh quantity of subconjunctival tissue, the very tissue which Kamel and I regard as the element in the spread towards the cornea of the pterygial process.

I will now be as honest as Dr. Gibson, who admits his recurrences. I worked out my pathology and technique, in the first place, through being honest, because I was not happy about the proportion of recurrences in the orthodox transplantation technique. Over the past three years I have had three recurrences. I have no doubt whatever about the cause. I attribute these recurrences to being overconfident about my own method and to not being careful enough in completely removing a layer of cornea.

If Dr. Gibson would do me the compliment of performing the operation exactly as described by me in *The British Journal of Ophthalmology* of February, 1948, I think he would be agreeably surprised.

Yours, etc.,

ARTHUR D'OMBRAIN.

135 Macquarie Street,
Sydney,
November 27, 1951.

MODERN TRENDS IN RADIOTHERAPY.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of November 24, 1951, Professor E. S. Meyers makes some interesting comments in reference to an article which appeared under my name in the issue of your journal dated November 3, 1951.

The relative infrequency of lymph node metastases in carcinoma of the lip in Queensland is chiefly due to the fact that the majority of the primary lesions are caused by sun exposure, and like cutaneous epitheliomata they are of low histological grading.

It is agreed that ten-year survival figures are desirable. The Queensland Radium Institute has only been in existence for seven years, but publishes in its annual reports the results of patients treated in the Brisbane Hospital since January 1, 1940.

In answer to Professor Meyers's question, it is my impression that for the routine treatment of cervical lymph node metastases few, if any, larger centres of radiotherapy overseas are using external radium therapy in preference to radical surgery. Even X-ray therapy, with the advantage of its much higher depth dosage, has few advocates in this particular condition.

At the Queensland Radium Institute it is the practice to advise extraction of teeth in the area contiguous to a lingual carcinoma. It is unfortunate that an occasional patient will throw away his chance of cure through reluctance to undergo a few extractions.

Professor McWhirter makes no claim to originality in treating over the last eight years carcinoma of the breast by simple mastectomy. There is, however, something original in his method of applying the post-operative X-ray therapy and in the adoption of a uniform approach by all the surgical staff of a large hospital.

Yours, etc.,

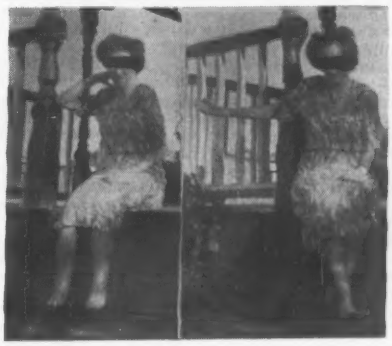
Queensland Radium Institute, Brisbane, November 30, 1951. A. G. S. COOPER.

ORTHOPÆDIC ASPECTS OF RHEUMATOID ARTHRITIS.

SIR: My congratulations to Dr. Colvin (November 3) for pointing out the importance of the orthopædic treatment of rheumatoid arthritis. A grave responsibility rests on the physician who treats a polyarthritic patient and does not apply these principles to each individual joint that is involved. The common unwillingness to use plaster of Paris is due, I think, to a fear of ankylosis. Dr. Colvin himself voices this fear when he says that, while osteoarthritic joints may be immobilized with safety, continuous immobilization of rheumatoid joints is precluded by the danger of ankylosis.

Paradoxically, continuous immobilization of painful and swollen rheumatoid joints increases their range by causing the arthritic process to subside. It is particularly useful for wrists, elbows, knees and metacarpo-phalangeal joints, any of which may be immobilized with complete safety for three to five weeks. Physiological use of the limb must be encouraged. After removal of the plaster the joint must be protected so that restoration of range is gradual—a sling for the elbow, a band caliper for the knee, a slab for the wrist.

In a girl whose wrists and left elbow have been ankylosed for years, the right elbow became swollen and increasingly painful three and a half years ago, with gradual restriction of range. After six months of ineffectual treatment, I applied plaster for three weeks with the elbow at right angles. The resultant range of completely painless movement is shown in the photographs, which show, too, the



ankylosed left elbow. A year after this a persistent painful effusion appeared in the right knee. A straight walking plaster was applied for four weeks; the effusion vanished and full range was soon restored to the knee.

Yours, etc.,

34 Queen's Road, Melbourne, November 23, 1951. M. KELLY.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 1, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.[2]	Australia[3]
Acute Rheumatism	..	..	..	..	..	..	..	..	..
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	..	11(10)	..	1	..	..	..	12
Diphtheria	3(3)	2(2)	5(3)	..	3(3)	2	..	..	15
Dysentery (Bacillary)	..	..	1(1)	..	..	..	..	..	1
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	10(6)	..	..	..	10
Infective Hepatitis	..	..	..	..	..	..	..	..	..
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	1(1)	..	..	..	1
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1	2(1)	..	..	..	1(1)	..	..	4
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	3(1)	7(3)	9(7)	34(27)	1(1)	2(2)	..	..	56
Puerperal Fever	..	..	..	..	2(1)	..	..	..	13
Rubella	..	11(10)	..	..	..	..	..	..	..
Salmonella Infection	28(11)	23(18)	2(1)	4(3)	2(1)	8(2)	..	..	67
Scarlet Fever	..	..	..	..	..	..	..	..	..
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	31(21)	11(6)	6(2)	9(6)	8(7)	9(4)	..	..	74
Typhoid Fever	..	1	1	..	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	3	..	..	..	..	..	3
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Northern Territory and the Australian Capital Territory.

PRE-BRONCHIECTASIS.

SIR: With reference to Dr. Piper's letter in the journal on November 17, 1951, though he appears to criticize me, I find on rereading it that he is apparently in agreement with me as regards treatment of these cases.

If he reads my paper again I think he will see that I have suggested the use of the more simple methods on these children first, but very strongly advocate bronchoscopic treatment in those cases which do not settle down with this. All cases in my paper came under the category he mentions in which my "treatment may be necessary and of avail". However, this is not such a small residue as he would suggest, and in such a large clinic as mine it mounts up to quite an appreciable number.

Why treatment which will prevent a patient becoming somewhat of a chronic invalid should be "economically impracticable" I fail to understand. Many of these patients were private patients and their remarks, as enumerated in my paper, show full satisfaction, while quite a number have stated that the cost is very low for the benefit obtained. As regards the public hospital patients, so far the authorities at the hospital where I work have not complained of the economic side, but, on the contrary, have expressed every satisfaction.

Having served for three years with the Field Artillery in the first World War, I may be credited with having some knowledge of the effect of shell fire on a sparrow. I agree with Dr. Piper that the effect is severe; but surely he would not compare a bronchoscopy with anything so extreme if he has ever seen it performed correctly. A bronchoscope, to be used efficiently, must be manipulated with great delicacy. The slightest heavy-handedness will hurt the patient, cause him to strain or struggle, and so militate against any benefit to be obtained by the treatment.

To see a child of six years of age cry, as I have done, because she thought she was not going to be bronchoscoped, under a local anæsthetic at that, should satisfy him that the procedure, if correctly done, is by no means drastic. Nor would he think so if he had seen a child of just four years of age who had not been bronchoscoped for nine months, but remembering the benefit he had previously obtained, ask his mother if he could be taken up for a further bronchoscopy when he developed a bad cold. He also had been done under local anæsthesia on his previous treatments. I might add that many patients, after my treatment, have asked why their various medical attendants had not instituted more active measures earlier instead of allowing them to run the risk of possibly developing an irreversible bronchiectasis.

Yours, etc.,

229 Macquarie Street, Sydney,
December 3, 1951.

H. B. HARWOOD.

Obituary.

GEORGE ALEXANDER EADIE.

WE regret to announce the death of Dr. George Alexander Eadie, which occurred on December 4, 1951, at Sandringham, Victoria.

Notice.

THE SYDNEY INSTITUTE FOR PSYCHO-ANALYSIS.

THE first seminar of the free introductory course for medical graduates provided by the Sydney Institute for Psycho-Analysis will be held on January 24, 1952, from 7 to 9 p.m. in the William H. Crago Council Chamber, British Medical Association House, 135 Macquarie Street, Sydney. Anyone interested in attending should write to the Secretary, Sydney Institute for Psycho-Analysis, 143 Macquarie Street, Sydney.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Tonkin, John Paul, M.B., B.S., 1951 (Univ. Sydney), 5 Arthur Street, Bellevue Hill.

Medical Appointments.

Dr. T. G. Ingram has been appointed municipal medical officer of health to the Latrobe Municipality, Tasmania.

Dr. T. C. Beard has been appointed medical officer of health to the Ross Municipality, Tasmania.

Dr. J. C. Mayo has been appointed honorary consulting radiotherapist to the Royal Adelaide Hospital.

Dr. W. Leggatt has been appointed medical officer at the Brisbane Mental Hospital.

Diary for the Month.

JAN. 8.—New South Wales Branch, B.M.A.: Council Quarterly.
JAN. 9.—Western Australian Branch, B.M.A.: Council Meeting.
JAN. 10.—South Australian Branch, B.M.A.: Council Meeting.
JAN. 11.—Queensland Branch, B.M.A.: Council Meeting.
JAN. 15.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
JAN. 22.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JAN. 25.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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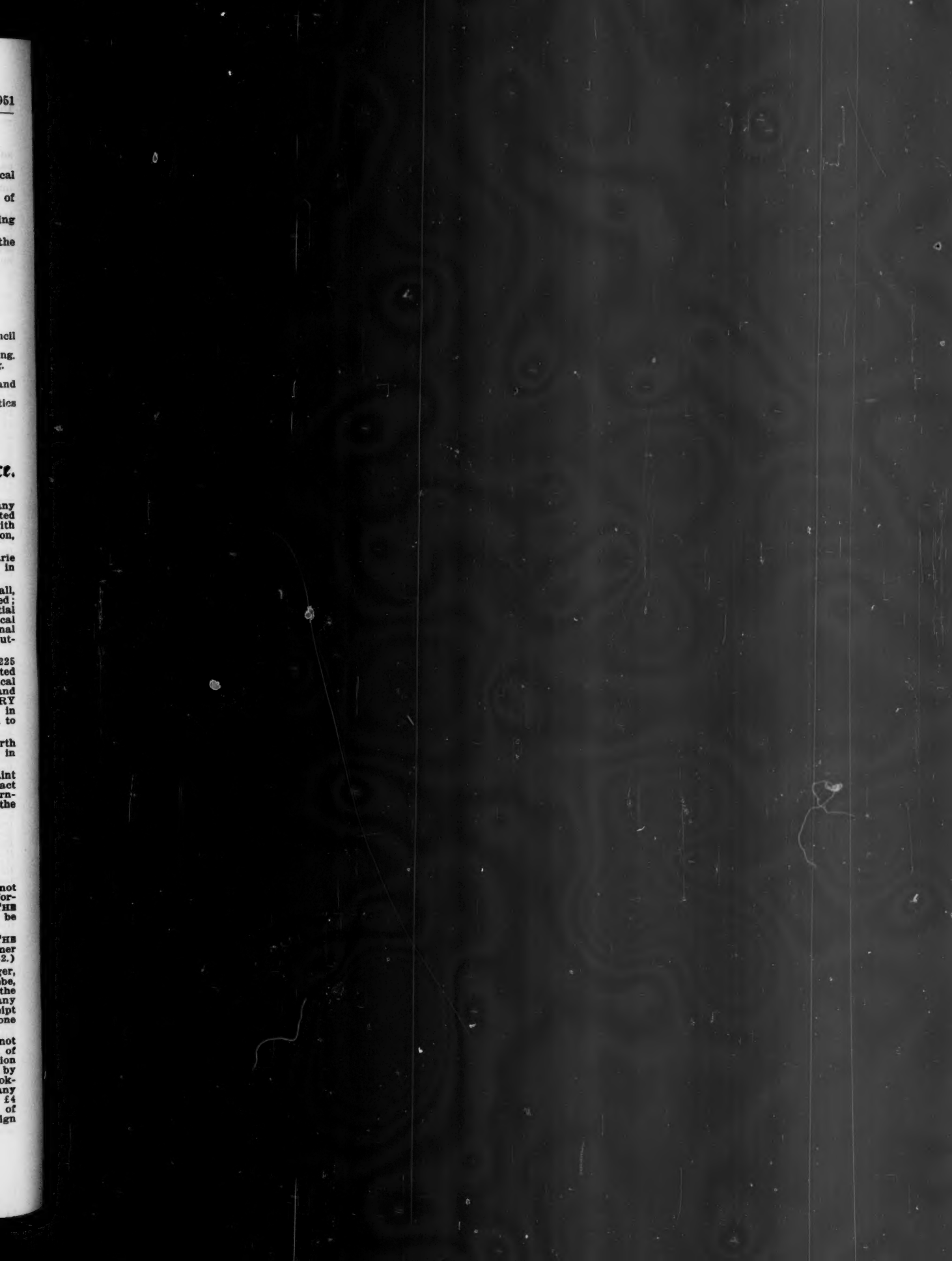

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VOL. II.—38TH YEAR. SYDNEY, SATURDAY, DECEMBER 29, 1951. No. 26.

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VICTORIA: Deputy Director of Health, 113 Queen Street, Melbourne.

QUEENSLAND: Deputy Director of Health, Anzac Square, Adelaide Street, Brisbane.

SOUTH AUSTRALIA: Deputy Director of Health, C.M.L. Building, 41-47 King William Street, Adelaide.

WESTERN AUSTRALIA: Deputy Director of Health, 4th floor, G.P.O., Perth.

TASMANIA: Senior Commonwealth Medical Officer, Howick Street, Launceston.

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THE HORNSBY AND DISTRICT HOSPITAL.

HONORARY MEDICAL STAFF NEW APPOINTMENT.

APPLICATIONS are invited for the appointment to the honorary medical staff in the undermentioned position for the unexpired portion of the present term which will expire on 1st September, 1952. Application forms are available from the hospital secretary and will close at 5 p.m. on Friday, 11th January, 1952. The position is Honorary Anæsthetist.—F. A. NAVEAU, Secretary and Chief Executive Officer, Box 7, P.O., Hornsby.

THE RYDE DISTRICT SOLDIERS' MEMORIAL HOSPITAL.

HONORARY MEDICAL STAFF.

The Board of Directors hereby invites applications in accordance with the by-laws and rules of the hospital for the following positions on the honorary medical staff for three years as from 1st February, 1952.

Honorary Consulting Surgeon.
Honorary Consulting Plastic Surgeon.
Honorary Consulting Physician.
Honorary Consulting Physician (out-patients).
Honorary Consulting Dermatologist.
Honorary Relieving Dermatologist.
Honorary Consulting Ear, Nose and Throat Surgeon.
Honorary Consulting Ophthalmic Surgeon.
Honorary Consulting Orthopædic Surgeon.
Honorary Relieving Orthopædic Surgeon.
Honorary Assistant Orthopædic Surgeon.
Honorary Consulting Urologist.
Honorary Relieving Urologist.
Honorary Consulting Radiologist.
Honorary Consulting Gynæcologist and Obstetrician.
Honorary Consulting Pædiatrician.
Honorary Consulting Anæsthetist.
Honorary Consulting Psychiatrist.
Honorary Consulting Visiting Medical Officer.
Honorary Visiting Medical Officer.
Honorary Assistant Visiting Medical Officer.

Applications on the prescribed form (which will be forwarded on request) close with the Secretary at 5 p.m. on 7th January, 1952.

THE ROYAL NORTH SHORE HOSPITAL OF SYDNEY.

HONORARY MEDICAL STAFF.

APPLICATIONS are invited for the following appointment to the honorary medical staff of the Royal North Shore Hospital for the balance of the current term, i.e., 31st July, 1954:

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Applications, accompanied by copies of at least two testimonials, should be made on the hospital's printed form which will be supplied on request.

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ADVERTISEMENTS.—Copy for advertisements in this section of the journal should be in the hands of the Manager ten days prior to date of publication. The rate is 25s. per single column inch, with a minimum charge of 10s.

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APPLICATIONS are invited for the position of Medical Superintendent, Normanton Hospital, at a salary of £1000 per annum together with basic wage variation of £57 10s. per annum and extra cost of living allowance at £75 per annum, also free residence, fuel and light, or £100 per annum in lieu thereof. Free board and lodgings to unmarried medical officer. Income tax concession "Zone A". Croydon and Burketown Hospitals are also administered by the Board and expenses are paid on necessary visits to these institutions. Applications should be forwarded air mail addressed to the Secretary.—W. A. PATCHING, Secretary.

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